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THE BACTERIOLOGY OF PEPTIC ULCERS AND GASTRIC MALIGNANCIES: POSSIBLE BEARING ON COMPLICATIONS FOLLOWING GASTRIC SURGERY

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INTRODUCTION

SURGEONS have always been aware of the danger of peritonitis following operations upon the stomach and duodenum. Freidrich and Weber[17] in a review of 207 subtotal gastrectomies for carcinoma reported a mortality of 25.1 per cent in which peritonitis was the cause of death in 70 per cent of these fatal cases. In resections for gastric ulcer 50 per cent of the deaths were due to peritonitis; whereas, in their duodenal ulcer cases only 20 per cent of the deaths were due to peritonitis. In spite of the fact that the operation of subtotal gastrectomy may have been performed with meticulous technique and that the intestinal sutures were carefully done, leaks along the suture line occasionally developed. These cannot always be ascribed to errors in technique. It was thought that some of the postoperative complications of this nature may be ascribed to the bacteriologic flora of the stomach and duodenum. Accordingly, an effort was made to make bacteriologic studies of the gastric and duodenal flora and peritoneal fluids during the operation and at various times thereafter.

The literature on the bacteriology of the stomach and duodenum in health and disease is voluminous. Cultures have been obtained (of gastric contents) by aspiration and from scraping and sectioning ulcers and carcinomas either at the operating table or post-mortem examinations. Numerous microorganisms have been recorded; namely,

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diplostreptococcus,[1] observed on spreads only, streptococci[2] of undetermined type, gram-positive diplococci[3, 4] as observed on spreads only, *Streptococcus viridans*,[5-7] enterococcus,[6, 9, 17A] *Staphylococcus albus* and *Staph. aureus*,[6] *Bacillus coli*,[6, 10, 13] *B. subtilis*,[8] *B. proteus*,[8] diphtheroids,[8] torula,[11] and gram-negative bacilli,[13] as observed on spreads. Various authors also have reported on the percentage of sterile cultures obtained. Appelmans and Vassiliadis[6] found sterile cultures in 10 out of 23 duodenal ulcer cases, 3 out of 17 gastric ulcer cases, and positive cultures in all gastric carcinomas. Their cultures were all obtained either from resected specimens by scraping the lesion with a platinum loop or from stomach contents. Streptococci were recovered by Rosenow[7] in 42 out of 54 cases of gastric ulcers (resected specimens). In 82 per cent of gastric ulcer cases and 92 per cent of duodenal ulcer cases Löhr[14] found the stomach or duodenal contents either to be sterile or to contain nonpathogenic organisms. However, he reported that 72 per cent of the gastric carcinomas yielded positive cultures, many of which were due to *B. coli*. Hewetson[11] in 1904 described a series of cultures of the stomach and jejunum taken at operation. Eighteen out of 36 stomach cultures and 16 out of 29 jejunal cultures were sterile. From this work Hewetson concluded that peritonitis following operations on the stomach and jejunum was caused by bacteria other than those present in these organs. This view has not been supported by the subsequent work of numerous authors. In 11 cases (4 gastric ulcers, 4 duodenal ulcers, 3 jejunal ulcers) Moutier[4] found the presence of *Str. viridans* in 10 instances. The relationship of gastric juice and hydrochloric acid upon the growth of microorganisms in vitro has also been exhaustively investigated. In his textbook Rehfuss,[8] quoting the work of Bartle and Harkins, includes a table listing the microorganisms compatible with various acid figures. Staphylococci are more resistant to hydrochloric acid than *B. coli* which in turn are more resistant than streptococci (type of streptococcus not mentioned in text).

It is evident from this review of previous investigators that there are no specific groups of microorganisms responsible for postoperative infections. The microorganisms have not always been completely identified.[1-4] In many instances the only descriptional terms employed were "gram-positive cocci," "tetrads," etc. If the cultures were obtained through a stomach tube, there was always the possibility of contamination with bacterial inhabitants of the mouth. In some studies only the spreads were examined without any attempt to culture the flora.[1-3] Meleney and associates[18] in a review of 106 cases of peritonitis (76 appendical, 10 related to small intestine, 6 to gall bladder, 6 to colon, and 8 miscellaneous) reported *B. coli* in 87 per cent, *Streptococcus viridans* in 49 per cent, and *B. welchii* in 38 per cent of the positive peritoneal cultures. No cases of peritonitis following subtotal gastrec-

tomy are included in this series so that although the bacterial flora was carefully and completely studied, it is of little significance in our problem.

In order to investigate the possible relationship of the bacteriology of the stomach and duodenum to postoperative infections, cultures were made from all specimens removed by subtotal gastrectomy. In many cases throat cultures and postoperative stomach cultures (obtained through a Levine tube) were also made. The cases were observed after operation for evidences of wound infections, intraperitoneal complications, peritonitis, and pulmonary complications.

METHODS

The specimens obtained by subtotal gastrectomy were received into a sterile basin from the operating table. With sterile instruments and gloves small sections of the serosa and mucosa were removed and placed in plain broth. A section was made of lymph glands if they were present, and when no nodes were palpated, a small segment of perigastric fat was excised for culture. If contamination of the serosa occurred during the operative procedure, only a specimen of mucosa was obtained. Sections were taken from either the ulcer bases or carcinoma lesions. When no ulcer was present in the resected surgical specimen (many ulcers adherent to or penetrating into the pancreas were left in situ), the mucosa immediately adjacent to the ulcer was used. Thus, in most instances the culture represented the bacteria present in the actual pathologic lesion. The specimens were then triturated without delay in the broth in which they were suspended and seeded into 1 per cent glucose broth, cooked liver broth under a vaseline seal, plain agar, ascitic fluid agar, blood agar and endo medium plates, and broth containing 1 per cent esculin (for the identification of enterococcus). All anaerobes were transplanted to fresh blood agar plates and cultured in anaerobic jars containing hydrogen for forty-eight to ninety-six hours.

Anaerobiosis was obtained in a tightly sealed jar from which the air was in part removed by a vacuum pump and subsequently the remainder of the air replaced by hydrogen under pressure in the presence of the catalytic agent, palladinized asbestos.[26, 27] The indicator for anaerobiosis was 0.1 c.c. of 1 per cent aqueous methylene blue in 10 c.c. of glucose broth which became colorless under anaerobic conditions. Various mediums used included Smith-Noguchi, Hiss serum sugar media (dextrose, mannite, maltose, lactose, saccharose), gelatin, litmus milk, and ascitic fluid agar. Surface and shake cultures were employed. Identification depended on staining characteristics, type of growth, fermentation of sugars, acid production, liquefaction of gelatin, coagulation of litmus milk, agglutination by specific sera, and tests for animal pathogenicity.

Gram-negative rods were further identified by fermentation reactions of mannite, maltose, dextrose, saccharose, and lactose, by the indol reaction, and finally by agglutination tests. Gram-positive bacilli producing fermentation, acid, and abundant gas in anaerobic cultures containing sugars were identified as *B. welchii* (*Cl. perfringens*) by typical morphology, liver damage,[28] positive rabbit-liver test,[28] gelatin liquefaction without lysis of coagulated protein[29] and well-pronounced capsule formation. *Staph. aureus* and *Staph. albus* were classified as A (pathogenic) or B (nonpathogenic) by the mannite fermentation, hemolysis on blood plates, and coagulase tests.[25] All streptococci were classified as either viridans (alpha), hemolytic (beta), or anhemolytic (gamma) (Brown[24]). Streptococci of the hemolytic variety were further grouped by precipitation reactions of the crude carbohydrate extracts with specific antisera (Lancefield[23]) and by their fibrinolysis of human fibrin described by Tillett.[22] All strains of *Str. hemolyticus* recorded in Tables I and VI were fibrinolytic and belonged to the Lancefield Type A pathogenic for man.

Acid titrations were made upon the stomach contents following a Rehfuss test meal and recorded in units of free and total acid. If no free acid was present, histamine was always administered subcutaneously.

RESULTS

A great variety of microorganisms were cultured from the specimens. These presumably pathogenic microorganisms listed in order of their frequency are *Str. viridans, Str. hemolyticus, Str. anhemolyticus, B. coli, B. welchii.* In addition, there were encountered diphtheroids, *Micrococcus catarrhalis,* and enterococcus, which are of rather doubtful pathogenicity; and also clearly saprophytic microorganisms as *B. subtilis,* yeasts, *Staph. aureus* and *Staph. albus* of B type.[25]

As may be seen from Table I, positive cultures were obtained in 93.7 per cent of gastric malignancies, 83.3 per cent of the gastric ulcers, 36.6 per cent of duodenal ulcers, and 37.9 per cent of secondary or complicated peptic ulcers. Presumably pathogenic microorganisms were recovered in 88 per cent of the malignancies and 30 per cent of the benign ulcer cases (as a group). In 24 cases in which the lymph nodes were cultured, 25 per cent were found to contain pathogenic microorganisms (71 per cent sterile) (Table I). Specimens of the serosa yielded pathogenic cultures in 15 per cent of 54 cases (37 were sterile) (Table I). Cultures of the perigastric fat (16 cases) were sterile in 11 and contained pathogenic microorganisms in 5 cases (31 per cent) (Table I). If contamination occurred in these 5 cases, it is important since it indicates contamination during the surgical procedure which then is a warning to the operator.

TABLE I

MICROORGANISMS CULTURED FROM MUCOSA, SEROSA, NODE, AND FAT IN VARIOUS TYPES OF LESIONS (85 CASES)
ACID FIGURES AT HEAD OF COLUMN

MICROORGANISM	GASTRIC ULCERS (6) AVERAGE FREE ACID UNITS, 58+ PATHOGENS, 50%					DUODENAL ULCERS AND EROSION (18) ULCER LEFT IN (12) AVERAGE FREE ACID UNITS, 64+ PATHOGENS, 17%					GASTRIC MALIGNANCIES (16) AVERAGE FREE ACID UNITS, 18- PATHOGENS, 88%				SECONDARY ULCER, BLEEDING ULCER, ETC. (29) AVERAGE FREE ACID UNITS, 58+ PATHOGENS, 31%					PREOPERATIVE SULFANILAMIDE (4)					TOTAL
	MUCOSA		SEROSA	NODE	FAT	MUCOSA		SEROSA	NODE	FAT	MUCOSA	SEROSA	NODE	FAT	MUCOSA		SEROSA	NODE	FAT	MUCOSA		SEROSA	NODE	FAT	
	ULCER	NO ULCER				ULCER	NO ULCER								ULCER	NO ULCER				ULCER	NO ULCER				
Str. viridans			1			1	1				10	2	2	1	1	1	1			1					22
Str. hemolyticus	2	1		1							4	1		1	1	1	1	1							14
Str. anhemolyticus						1					3	1	1	1	2										10
Escherichia coli											6	1			1										8
Clostridium perfringens *(B. welchii)*						1					3	1			1	1	1								8
B. friedländeri											1														1
Staph. albus (A)						1		1			3	1		1											7
Staph. aureus (A)						1				1					1	1									4
Enterococcus											1														1
Staph. albus (B)	1					3	2	4		1	3			1	2	2	2								21
Staph. aureus (B)						1	1					1					1		1						5
Corynebacterium hodgkinii	1					4		2		1	2				2	1			1						14
Saccharomyces						1					1				1	1	1		1						6
B. subtilis	1					2				1	2	1			1										8
Neisseria catarrhalis															1		1								2
Sterile	1					6	5	16	5	3	1	9	9	5	7	4	11	3	3	2	1	1			

TABLE II

STOMACH CULTURES TAKEN BY LEVINE TUBE AFTER OPERATION (62 CASES)

B. coli	46
Enterococcus	29
B. friedländeri	5
Str. hemolyticus	4
Str. anhemolytic	3
Str. viridans	2
B. welchii	4
Staph. aureus (A)	4
Staph. aureus (B)	2
Staph. albus (A)	1
Staph. albus (B)	6
B. proteus	3
B. pyocyaneus	3
B. subtilis	3
Neisseria catarrhalis	2
Corynebacterium hodgkinii	1
Saccharomyces	1

Cultures of the stomach contents obtained by Levine tubes within twenty-four hours after subtotal gastrectomy were made in 62 cases and are summarized in Table II. *B. coli* was cultured forty-six times and enterococcus twenty-nine times in addition to a great variety of other microorganisms. No cultures were sterile. It may be stated, therefore, that following subtotal gastrectomy, the flora of the stomach closely resembled that of the intestinal tract below the duodenum regardless of the type of lesion encountered or the preoperative acid figures. Thus one may deduce that a free exchange of bacteria occurs at the gastroenterostomy stoma.

Throat and stomach cultures with particular reference to *Str. hemolyticus* were performed in 41 patients. These cultures were taken over a period of two years. Positive throat cultures were obtained each month as follows: Jan. 2, Feb. 3, March 2, April 3, June 1, Oct. 2, Nov. 1, and Dec. 1. In only 3 cases (7.3 per cent) was there found *Str. hemolyticus* in the throat and stomach of the same individual. On the other hand, 12 patients had *Str. hemolyticus* in the throat and no hemolytic streptococci in the stomach. In this series the presence of hemolytic streptococci in the throat apparently had no significant bearing to the incidence of complications.

Table I shows the relation between free acid figures obtained by Rehfuss test meal and the percentage of significant cultures present. The outstanding fact is the high percentage (88 per cent) of presumably pathogenic microorganisms present in the carcinoma cases in which the acid figures are extremely low. In the simple and complicated ulcers the acid figures were very similar, but the percentage of significant positive cultures varied from 17 per cent in the simple duodenal ulcers to 50 per cent in simple gastric ulcers. One must assume, therefore, that the actual amount of free acid present in the stomach is not an important determining factor which controls the bacterial flora of the

gastric and duodenal lesions. Horsley,[20] Lahey,[21] and others have suggested preoperative lavage and instillation of weak hydrochloric acid solution in carcinoma cases in an effort to sterilize the stomach. The bacteriologic studies herein reported support the view that carcinoma cases have a very high percentage of positive cultures (93 per cent). Further study using our method of taking cultures of operative specimens as already described under Methods is necessary to state accurately whether there would be a decrease in the number of microorganisms and postoperative infections with their routine.

An attempt was then made to correlate these operative bacteriologic findings with the postoperative course of the patients. The possible relationship between the type of microorganisms and the postoperative complications is made in Table III. The observations seem to show

TABLE III

MICROORGANISMS AND CLINICAL COURSE CORRELATED

MICROORGANISMS CULTURED AT OPERATION IN CASES DEVELOPING COMPLICATIONS	NUMBER OF COMPLICATIONS THAT DEVELOPED							
	WOUND INFECTIONS (12)	INCIDENCE	PULMONARY COMPLICATIONS (16)	INCIDENCE	ABDOMINAL COMPLICATIONS (16)	INCIDENCE	MORTALITY (15)	INCIDENCE
Str. viridans	5	5/22	2	2/22	2	2/22	7	7/22
Cl. perfringens (*B. welchii*)	3	3/ 8	2	2/ 8	3	3/ 8	3	3/ 8
Str. hemolyticus	2	2/14	1	1/14	2	2/14	3	3/14
E. coli	3	3/ 8	2	2/ 8	3	3/ 8	1	1/ 8
Str. anhemolytic	2	2/10	1	1/10	3	3/10	0	
Staph. albus (A)	0		2	2/ 7	0		0	
Staph. aureus (A)	0		0		0		1	1/ 4
Enterococcus	0		0		0		1	1/ 1
B. friedländeri	0		0		0		0	
Staph. albus (B)	1	1/21	1	1/21	1	1/21	1	1/21
B. subtilis	1	1/ 8	1	1/ 8	1	1/ 8	0	
Staph. aureus (B)	0		0		0		0	
Corynebacterium hodgkinii	0		1	1/14	0		0	
Saccharomyces	0		1	1/ 6	0		1	1/ 6
Neisseria catarrhalis	0		0		0		0	
Sterile	1		4		1		3	

that there was a greater incidence of wound and intra-abdominal infections in those cases in which positive cultures were obtained at operation. The presence of *Str. viridans, B. welchii, Str. hemolyticus, B. coli,* and *Str. nonhemolyticus* (i.e., indifferent gamma of Brown) alone or in combination were particularly significant. Considering the individual complications, the microorganisms listed above were present alone or in combination in 9 out of 12 patients (75 per cent) with wound infections, 12 out of 16 patients (75 per cent) with intra-abdominal complications, 10 out of 15 (66⅔ per cent) of the deceased patients, and in only 6 out of 16 patients (37.5 per cent) with pulmonary complications.

TABLE IV

PREDOMINANT MICROORGANISMS PRESENT IN WOUND INFECTIONS
(CULTURES IN 8 CASES)

Staph. aureus (A)	2
B. welchii, B. coli	3
Enterococcus, *B. coli*	1
B. welchii, Str. hemolyticus	1
B. proteus	1

In Table IV are listed the important microorganisms cultured from wounds in 8 cases which developed wound infections (4 wound infections not cultured). In 3 of these 8 the similarity between the stomach and wound cultures was either partial or complete. One wound infection showed *Str. hemolyticus* and in this case neither the stomach nor throat contained this microorganism.

However, even without close correlation of the bacteriology in wound infections in these cases, one may assume that the presence of these microorganisms in the stomach and duodenum predisposes to postoperative complications related to the operative site (duodenal leak, peritonitis, and wound infections).

In an analysis of the 15 fatal cases (Table V) 8 deaths (53 per cent) could be ascribed to intraperitoneal infections (5 proved by post-mortem, 2 by abdominal puncture, and 1, clinically). Of the remaining 7 patients, 1 died of bronchopneumonia; 1 of functional obstruction; and the cause of death was not definitely determined in 5 patients upon whom no post-mortem examination was performed. In the 8 patients succumbing to peritonitis, the following microorganisms were cultured from the operative specimens: *B. welchii* (3 times), *Str. hemolyticus* (4 times), *Str. viridans* (5 times), which seemed then of importance in consideration of postoperative mortality from peritonitis. It is also of interest to note that in 5 deceased patients in whom death could not be definitely ascribed to peritonitis, *B. welchii* was present in cultures other than those taken of specimens at operation (one obtained by abdominal puncture postoperatively, one at post-mortem, one by stomach tube postoperatively, and two in wound infections).

In our series one is impressed by the fact that in the 7 cases in which *B. welchii* was cultured, morbidity and mortality rates were higher. Every patient in whom *B. welchii* was recovered at operation either developed some serious complication or died. It seems reasonable, therefore, to assume that if this microorganism is present, potential danger exists and may be of significant prognostic value. Following subtotal gastrectomy there is always a certain amount of devitalized tissue upon which these anaerobic organisms thrive. As a result, a dehiscence either of the duodenal closure or the enterostomy suture line occurred in 5 cases with subsequent leak (1 case) and localized peritonitis with subphrenic abscess (1 case) or generalized peritonitis and death (3 cases). As has

TABLE V

ANALYSIS OF ALL DECEASED CASES

LESION	CAUSE OF DEATH	CULTURES AND REMARKS
1. Lymphosarcoma*†	Peritonitis; dehiscence of all suture lines	*B. welchii, Str. hemolyticus, Str. viridans*
2. Infiltrating adenocarcinoma with nodes*†	Peritonitis; bronchopneumonia	*Str. hemolyticus, Str. viridans, (B. welchii, B. coli* at post-mortem)
3. Infiltrating scirrhous; adenocarcinoma with nodes†	Peritonitis clinically; no post-mortem	*Str. hemolyticus, Str. viridans (B. welchii,* Levine tube postoperatively)
4. Infiltrating adenocarcinoma	Cause (?); no post-mortem	*B. coli,* enterococcus
5. Adenocarcinoma*†	Peritonitis; (*B. welchii* invasion of jejunum, dehiscence of duodenal stump)	*Str. viridans* (premortem abdominal aspiration *B. welchii)*
6. Secondary gastrectomy for jejunal ulcer†	Peritonitis (no post-mortem) (abdominal culture at death revealed pus)	*B. welchii, Str. viridans*
7. Secondary gastrectomy (chronic duodenitis); no ulcer on specimen	Cardiac (?); second day after operation; no post-mortem	Sterile at operation
8. Bleeding duodenal ulcer (chronic gastritis, ulcer left in)*†	Peritonitis (duodenal leak) (*B. coli* and enterococcus at post-mortem)	*Yeast (B. welchii* in wound)
9. Secondary gastrectomy for chronic gastric ulcer	Rheumatic cardiac (?) (died third day; no post-mortem)	*Str. hemolyticus, Str. viridans*
10. Bleeding ulcer	Hemorrhagic bronchopneumonia; abdomen clean, sutures intact	*Staph. albus (B)*
11. Secondary gastrectomy*†	Peritonitis; dehiscence of duodenal stump	*B. welchii;* post-mortem *B. welchii* and *B. coli*
12. Gastrectomy (secondary) and entero-enterostomy	Functional obstruction with vomiting, alkalosis, etc.	Sterile *(B. welchii, B. coli* in wound)
13. Chronic peptic ulcer	Pneumonia; peritonitis(?); no post-mortem	Sterile
14. Chronic duodenal ulcer†	Metastatic *Str. hemolyticus* peritonitis (from throat); no post-mortem	*Staph. aureus (A)*
15. Polypoid carcinoma with nodes	Died second day postoperative; shock; temperature, 106.8° F.; abdomen scaphoid; no post-mortem	*Str. viridans* and *Corynebacterium hodgkinii*

*Proved by post-mortem examination.
†Death ascribed to peritonitis.

already been stated in the introduction, a great number of microorganisms have been reported as being cultured from the stomach and duodenum, but *B. welchii* has not been previously recorded to our knowledge. Freidrich and Weber,[17] for example, reported cultures on 25 gastric cases in which no anaerobes were recovered.

We feel that the finding of *B. welchii* in the cases herein reported was unexpected and of real clinical significance when found.

DISCUSSION AND CONCLUSIONS

The bacteriologic studies reported suggest several precautions and therapeutic innovations in operations on the stomach and duodenum in an effort to avoid postoperative morbidity and mortality.

1. Contamination of the peritoneal cavity and abdominal wall by gastric and duodenal contents should be avoided in view of the possible infectivity of these contents (93 per cent of the gastric malignancies, 83 per cent of the gastric ulcers, etc., showed positive cultures from the lesions which are in turn bathed by intralumenary fluids).

2. Inasmuch as 25 per cent of the nodes may contain microorganisms of presumable pathogenicity, one should treat the nodes and material contained in them as potentially infective.

3. Drainage of the peritoneal cavity down to the duodenal stump (to allow avenue of escape if leak occurs) or site of gross contamination by means of a lateral stab drain seems advisable, especially when there is some doubt as to the reliability of the suture lines. Whether the duodenal ulcer is completely excised or left in situ *(äuschaultung)*, the line of stomach resection, if feasible, should be made far enough away from the actual ulcer. This should be done because these tissues are less infected and healing is therefore better. The digestive action of pancreatic ferments, undue tension, and interference with blood supply are certainly important factors which contribute to the reliability or lack of security of the duodenal stump closure. The presence of pathogenic bacteria at or near the suture line may be another factor.

4. Since 93 per cent of the gastric malignancies had positive cultures, an "aseptic" method of resection similar to that used in colonic resection may be of advantage in gastric carcinoma cases. The Petz[30] or similar apparatus may solve this problem.

5. In view of possible *B. welchii* infection in a certain number of cases, tension at suture lines or strangulation of tissue may prove dangerous (7 of 85 cases had *B. welchii* present which organism thrives on dead tissue). The use of *B. welchii* antitoxic sera prophylactically and therapeutically in gastric cases is being seriously considered provided, of course, sera of sufficient potency may be secured.

6. In view of previous experience with sulfanilamide as a preventive measure against peritonitis in colon surgery,[19] this drug now is being

administered to a series of gastric cases before operation. Since sulfanilamide is effective against the *Str. hemolyticus* and has also been used with some success both clinically[31, 32] and experimentally[31, 33, 34] against *B. welchii*, it may prove of real value, particularly in the carcinoma cases which are heavily infected with both of these pathogens.

SUMMARY

1. Pathogenic microorganisms are frequently present in gastric and duodenal lesions (88 per cent of the malignancies, 30 per cent of the benign ulcers).

2. Postoperative complications and mortality rates appeared higher in cases with pathogenic microorganisms (streptococci of all varieties, *B. welchii*, *B. coli*, alone or in combination).

3. *B. welchii* indicate a grave prognosis when cultured from the stomach and duodenum at operation.

4. Low gastric acidity and a high percentage (88 per cent) of pathogenic microorganisms in carcinoma cases are noteworthy.

5. Cultures of the stomach after subtotal gastrectomy show intestinal microorganisms.

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LEIOMYOMA MALIGNUM OF THE STOMACH

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NEOPLASMS of the smooth muscle of the stomach may be classified as: (1) benign leiomyoma, (2) leiomyoma malignum, (3) metastasizing leiomyoma, and (4) leiomyosarcoma. It is our purpose in this paper to report a gastric leiomyoma which had characteristics that stamped it as malignant and whose picture did not conform with that of a sarcoma.

In 1936 Conway[1] collected reports of 56 cases of leiomyoma of the stomach and added 2 cases of his own. These tumors were encapsulated and nodular and bulged on section of the surface. Some were external and projected into the peritoneal cavity; others were internal and invaded the lumen of the stomach and occasionally were accompanied by mucosal ulcerations. The tumors varied in size and were sometimes multiple. The distribution as to sex was practically equal. Some of the tumors caused pyloric obstruction. Conway failed to include the gastric leiomyomas reported by Down,[2] Meyer and Rosi,[3] Martinez and Minnhaar,[4] Villata,[5] Willis,[6] Davidson,[7] Leon,[8] McCarthy,[9] Denham,[10] Kohno,[11] Zakharov,[12] and Millar.[13] The studies of Rieniets[14] would seem to indicate that leiomyoma of the stomach is much more common than has been thought. In the first 100 consecutive post-mortem examinations performed at the Mayo Clinic in 1928, 21 leiomyomas were found in 16 stomachs. A second group of 100 stomachs were found to contain 22 leiomyomas in 16 stomachs. Thirty-four additional leiomyomas in 30 stomachs were found in a third group of unmentioned size. In all, 77 leiomyomas were found in 62 stomachs. In 50 cases there was a single tumor; in 9 cases, 2 tumors; and in 3 cases, 3 tumors. There were 43 males and 19 females. The average age was 59.17 years. Rieniets[14] described a fourth group of 21 leiomyomas removed at operation. In 14 of these cases the tumors were removed primarily because of their size and 7 were removed secondarily in the course of other operations. The average age in these cases was 51.48 years.

In 1932 Melnick[15] reported a case of benign metastasizing leiomyoma of the stomach in which there were metastases in the liver. Davidson[7] describes the x-ray signs of gastric leiomyoma as: "(1) regular filling defect usually between intact curvatures (particularly with submucous growths); (2) signs of external pressure (particularly in pedunculated

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subserous growths); (3) abnormally devious but intact rugae (particularly in submucous growths); (4) crater formation (where ulceration has occurred); (5) block in peristalsis (particularly in mural types); (6) filling defects in other organs (notably in duodenum in intragastric pedunculated growths); and (7) obstruction at cardia and pylorus."

Since the publication of Conway's paper, cases of gastric leiomyoma have been reported by Mallory,[16] Lindquist and Mock,[17] Hartman and Camp,[18] Mott,[19] Sworn and Cooper,[20] Toland and Kroger,[21] and Collins and Collins.[22] Pure leiomyomas of the stomach were found 6 times during the period from Jan. 1, 1936, to Nov. 28, 1940, at the Evanston Hospital. They occurred twice in the examination of 7,827 general surgical specimens and 4 times in 653 necropsies, a total incidence of 0.07 per cent.

CASE REPORT

M. H., aged 11 years, was admitted to the Evanston Hospital on Oct. 3, 1938, complaining of vomiting of two days' duration and a mass in the stomach. The history was as follows: The child was delivered normally and had had an entirely uneventful period of growth and development up to the present time. On Aug. 25, 1938, she had a bout of "intestinal flu," during which she had postcibum vomiting for five days. This cleared up with the use of barley water. There were no other associated abdominal symptoms. At noon on Oct. 2, after having taken canned peach juice, the patient had an attack of nonprojectile involuntary emesis of brown fluid; this was not preceded by nausea. At 7:00 P.M. of the same day she vomited again, several hours after having eaten dinner. At 2 o'clock the following afternoon (the day of admittance to the hospital) she again vomited and the material was found to contain blood.

Inventory by systems showed a loss of 4 pounds in weight during the attack of vomiting in August. This had been regained. There were no symptoms referable to the head or to the cardiorespiratory system. There were no gastrointestinal symptoms other than those referred to, no change of appetite, no food sensitivity, no belching. There were no genitourinary or neuromuscular symptoms. The patient had had measles three years previously. Her tonsils and adenoids had been removed when she was 3 years old.

Physical examination revealed a well-developed, moderately well-nourished, intelligent, cooperative girl, who was apparently in excellent health. The only significant findings were a slightly injected pharynx and cervical lymph glands that were small, discrete, firm, and bilaterally palpable, being more marked on the left side. The chest and heart were normal. The abdomen showed no marked tenderness or rebound phenomena. In the epigastrium there was palpated an elongate, firm, movable, nodular, slightly tender mass, about 2½ by 1½ inches, which seemed to be in the pyloric end of the stomach and which moved with respiration. The abdomen was not distended, but there was some fullness in the right upper quadrant. No peristaltic waves or dilated waves were seen. The abdominal sounds were normal. There were a few palpable inguinal glands. The reflexes were physiologic. No other significant findings were elicited.

X-ray examination revealed a tumor mass encroaching on the duodenal bulb, antrum, and body of the stomach from the lesser curvature. It could not be determined whether the tumor was intrinsic or extrinsic and what its nature was.

Examination of the blood showed 4,390,000 red blood cells, 90.9 per cent hemoglobin, and 9,250 white blood cells. Examination of the emesis fluid revealed a few red blood cells but a plus-3 benzidine test. The feces and urine were normal.

The diagnosis was gastric neoplasm of unknown nature.

Laparotomy was performed on Oct. 4, and a large tumor presented on the outside of the lesser curvature and a tumor mass projected into the cavity of the stomach from the lesser curvature. Gastric resection (Hofmeister-Polya) with anastomosis of the jejunum and proximal portion of the stomach was carried out. The patient was given 250 c.c. of blood during the operation and 250 c.c. postoperatively. No postoperative Wangensteen suction was employed. The patient made an entirely uneventful recovery.

On June 18, 1940, the patient was in fine health and weighed 91¼ pounds, a gain of 21¼ pounds since November, 1938. There was no evidence of recurrence on physical or x-ray examination at that time. Twenty-five months after the operation was performed the patient was well and was clinically relieved of the disease. The prognosis, however, is guarded.

The pathologic report on the specimen removed was as follows:

Gross Description.—The resected portion of the stomach consisted of the pylorus and antrum and a portion of the fundus (Fig. 1). The greater curvature was 13 cm. long; the lesser curvature, 11 cm. long. A nodular tumor mass arose from the lesser curvature and 2 to 3 cm. of the adjacent anterior and posterior walls of the stomach. Toward the pyloric end the tumor grew outward for a distance of 2.5 to 3 cm. to form daughter nodular masses and, at a point approximately 4.5 cm. from the pylorus, it measured 4.5 cm. Numerous engorged blood vessels coursed over the tumor beneath the granular, yellow-pink serosa of the stomach. The red to yellow-gray capsule was 1 to 2 mm. thick. The anterior portion of the large tumor presented a subcapsular cyst 2.5 by 2 cm. Two to three centimeters of the fatty gastrocolic ligament was attached to the specimen. Numerous engorged, tortuous vessels passed from the gastrocolic ligament into the wall of the anterior and posterior surfaces of the stomach.

When the stomach was opened (Fig. 2), a smooth, oblong tumor was seen projecting into the lumen. The distal border abutted against the pylorus. This tumor was 7 cm. long and 3 cm. wide and protruded 1.5 to 2 cm. into the lumen of the stomach. It was covered with a smooth, yellow-pink mucosa. The summit of this tumor presented a recent hemorrhagic erosion of the mucosa, measuring 12 by 10 mm. The muscularis of the pylorus was 6 mm. thick; the mucosa, 2 mm. thick; and the muscularis of the fundus, 3 mm. thick. The mucosa was thrown into folds 10 mm. high. Except for the aforementioned features, the remainder of the normal gray-pink mucosa presented numerous rugae. The intragastric tumor was situated in the magenstrasse and bulged more toward the anterior than toward the posterior surface.

Bisection of the extragastric tumor protruding from the lesser curvature exhibited a fleshy, yellow-white, semifirm, fairly homogeneous structure with an occasional small area of cystic degeneration. Three cysts, measuring from 10 to 20 mm. in diameter, were lined with glistening neoplastic tissue and filled with bloody serous fluid. The small contiguous daughter nodules were composed of homogeneous material similar to that described in the first mass. The intrinsic tumor was contiguous with the extrinsic tumor.

Microscopic Description.—Sections from the intragastric portion of the tumor presented one margin covered by an intact gastric mucosa (Fig. 3). The engorged, edematous interstitial tissue of the membrana propria exhibited a slight round-cell infiltration. The normal muscularis mucosae in this section could easily be identified. A narrow layer of edematous submucosa separated the muscularis

Fig. 1.

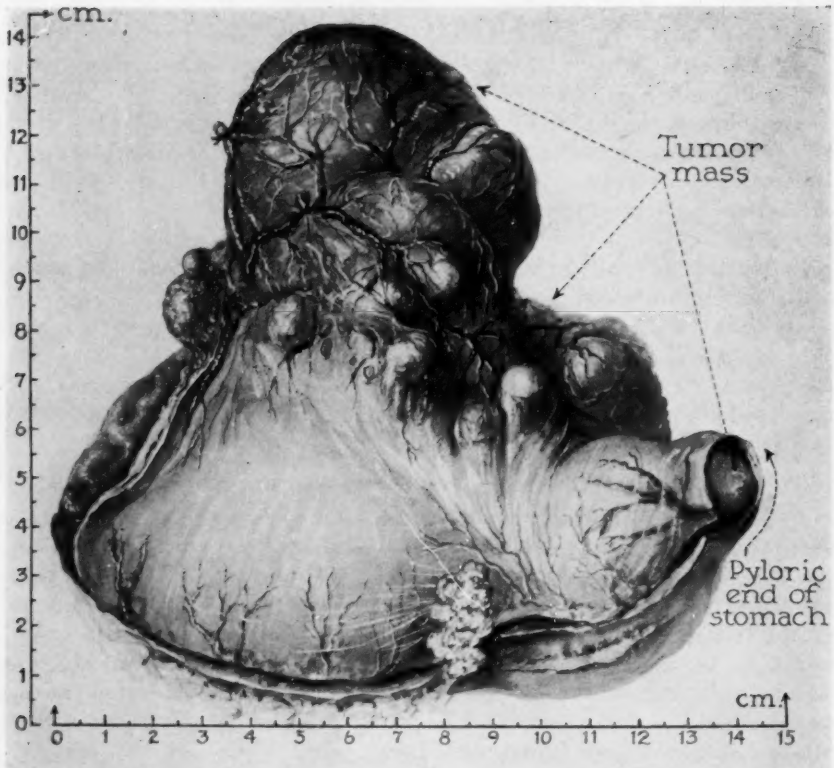

Fig. 2.

Fig. 1.—Leiomyoma malignum. Appearance of resected portion of the stomach.
Fig. 2.—Leiomyoma malignum. Appearance of opened stomach.

mucosae from the upper margin of the tumor. The tumor contained a moderate number of thin-walled, small, slitlike to oval endothelial-lined spaces. In the main the tumor was composed of anaplastic mesenchymal cells exhibiting considerable hyperchromatism, numerous mitotic figures in the prophase, and slight variation in size and shape (Fig. 4). The numerous anaplastic cells had an irregular, round to oval, smudgy, basophilic nucleoplasm surrounded by a blue-pink, homogeneous

Fig. 3.—Leiomyoma malignum. Section showing covering of intact gastric mucosa.

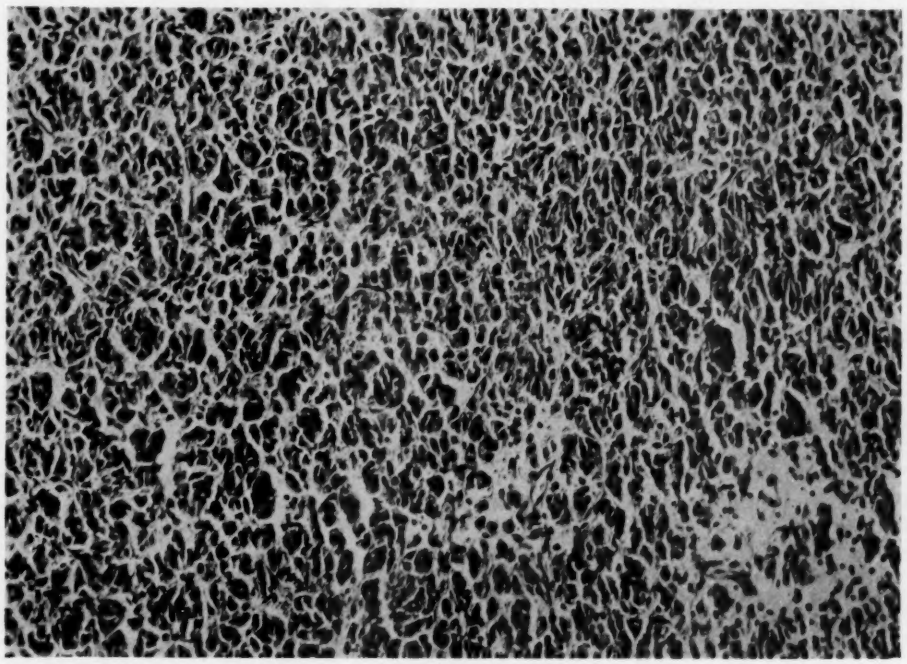

Fig. 4.—Leiomyoma malignum. High power section.

cytoplasm. The more mature cells were elongated and resembled smooth muscle cells. Their blunt, cigar-shaped nuclei presented a uniform distribution of basophilic chromatin with pale blue interstices, a definite nuclear membrane, and an occasional deeper blue-black nucleolus located near one pole. Slender, fibrillar, pink cytoplasmic processes arose from the more mature cells. The latter were growing in bundles or interlacing fasciculi separated by a delicate fibrous connective tissue and small capillaries. Occasionally the more anaplastic cells exhibited multinucleated giant cells.

Masson's trichrome stain identified the tumor cells as composed of smooth muscle. Delicate myoglia fibrils were demonstrated in the more mature muscle cells. Mallory's phosphotungstic-acid hematoxylin stains, although unsatisfactory, revealed blue myoglia fibrils.

Sections from the pyloric wall contained normal mucosa and an edematous, widened submucosa with engorged vessels and hypertrophy of the muscularis. No tumor cell emboli were seen in the veins or lymphatics.

Although no metastases were apparent during the operation on this child, it is thought that the diagnosis of malignant leiomyoma is compatible with the gross and microscopic features present in the tumor.

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THE EFFECT OF COLLOIDAL ALUMINUM HYDROXIDE ON CERTAIN ASPECTS OF BLOOD COAGULATION

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IN RECENT years colloidal aluminum hydroxide has been advocated clinically in the treatment of bleeding peptic ulcer.[1, 2] At the same time it has been advocated in the laboratory for the total inactivation of prothrombin from blood plasma.[3] As prothrombin-free blood is incoagulable under physiologic conditions, it seemed important to determine whether the anticoagulant properties of aluminum hydroxide had any practical effect on bleeding time in the experimental animal. Furthermore, the closely related substance, aluminum oxide, was found by Dam and Schønheyder[4] to reduce the activity of vitamin K concentrates under certain conditions. Consequently, before giving patients aluminum hydroxide over long periods of time, it seemed worth while to determine whether it might have a destructive effect on vitamin K under controlled dietary conditions. The following experiments were performed to answer these questions.

EXPERIMENTAL

Two commercial aluminum hydroxide preparations were tested. They were creamalin (Alba Chemical Co.) and amphojel (Wyeth). Both preparations contain finely divided aluminum hydroxide with flavoring material. One part of either of these compounds was found to inactivate the prothrombin in ten parts of human or dog plasma after five minutes' shaking. The prothrombin determinations were done by the method of Quick.[3]

Experiments on Bleeding Time in Dogs.—The effect of amphojel and creamalin on the duration of bleeding from skin incisions was measured as follows: Healthy dogs were anesthetized by the administration of sodium amytal intraperitoneally and the abdominal walls were cleanly shaved. Incisions 2 cm. long were then made through the skin in pairs. The two incisions were placed equal distances from the linea alba but on opposite sides. One incision of each pair was used to test the effect of an aluminum hydroxide preparation on bleeding time and the other was treated in the same manner with physiologic saline solution as a control. It was believed that untreated incisions would not provide a fair control because the effect of evaporation might hasten coagulation. It was anticipated that a suspension of particles would tend to hasten

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coagulation, but as a suspension of any material other than aluminum hydroxide would introduce a new variable, it was decided to use physiologic saline solution in the control experiments.

The amphojel, creamalin, and saline solution were applied to the incisions by a slow drip from separatory funnels placed just above the skin level. The rate of drip in the test and control incisions was the same. In each dog care was taken to apply the test substances to some incisions on the right side and to others on the left side. The blood was sponged away from the animal's flanks when it ran down, but the incisions themselves were not sponged. The bleeding time was measured from the time of incision to the time the blood stopped flowing. The fluids that dripped on the wound tended to wash away some red cells from the clot even after bleeding had stopped, but the end point was reasonably distinct.

The 68 control incisions bled for an average of 6 minutes and 32 seconds. The 68 incisions treated with one or the other of the aluminum hydroxide preparations bled an average of 12 minutes and 42 seconds, or an increase of 94 per cent. The 43 incisions treated with amphojel bled for a mean period of 13.7 minutes and the 25 incisions treated with creamalin bled for a mean period of 10.9 minutes.

The effect of these preparations was then tested on incisions made in the mucosa of the small bowel. In some of the animals the loops of the bowel were exteriorized with an intact blood supply after preliminary enteroenterostomy and the exteriorized loop opened after the wound had healed. In other animals acute experiments were done. A loop of jejunum was drawn out and opened along its antimesenteric border, and the mucosal incisions were made at once.

In all of these experiments the parallel pairs of incisions were placed at approximately equal distances from the mesenteric attachment. The incisions were about 1 to 1.5 cm. in length. The mean bleeding time from 14 control incisions was 61.4 seconds. The mean bleeding time from 8 incisions treated with creamalin was 61.6 seconds.

Experiments on the Effect of Aluminum Hydroxide on the Activity of Vitamin K.—K avitaminotic white rock cockerels were obtained by growing one-day-old birds in false-bottom cages on Ansbacher's K_1 diet.[5] The water was changed three times a day and fresh diet was supplied twice daily. After eight days blood from the cervical vessels of sample chicks was collected in evaporating dishes. Coagulation time exceeded thirty minutes, the criterion of K avitaminosis accepted by Ansbacher. Thirteen of the chicks were then given vitamin K in the form of cerophyl in the proportion of one part to one hundred parts of diet. Cerophyl is a preparation of dried cereal plants which has been used by us as a source of vitamin K.[6] The amount used was at least four times the amount necessary to protect chicks from K avitaminosis. Another group

of 17 chicks was given the same amount of cerophyl to which had been added creamalin. The resulting diet contained Ansbacher's K_1 diet,* one hundred parts; cerophyl, one part; and creamalin, ten parts. After four days 3 chicks from each of the three groups were tested for K avitaminosis. Those on the Ansbacher diet alone showed clotting times of over thirty minutes. Those with the 1 per cent cerophyl supplement had clotting times of less than ten minutes, and those of 1 per cent cerophyl plus 10 per cent creamalin also had clotting times of less than ten minutes.

It was evident from these results that creamalin did not interfere with the action of vitamin K in the form of cerophyl in the proportions used, and the proportions were selected with an excess of the aluminum hydroxide preparation and a very moderate dose of vitamin K. As these two ingredients were thoroughly mixed before being added to the Ansbacher diet, there was every opportunity for the action of creamalin.

The remaining birds which had not received vitamin K were treated with 2-methyl-1, 4-naphthoquinone in the proportion of one part per million of diet. Four of the 6 birds received a 50 per cent supplement of creamalin which was mixed with the vitamin K substitute before being added to the diet. The 2-methyl-1, 4-naphthoquinone had a curative effect in all of the chicks regardless of whether or not aluminum hydroxide was present. The findings in this small group of chicks confirmed the experiments in which cerophyl was used.

DISCUSSION

The difference in the bleeding time of the skin incisions treated by the aluminum hydroxide preparations seems rather striking, but the variations in individual bleeding times were so great that the results do not have statistical significance; that is, the difference of the means is less than twice the standard error of the differences.

The bleeding time of incisions in the jejunal mucosa appeared not to be influenced by the application of an aluminum hydroxide cream. Neither of the conditions used approximates the bleeding which takes place in certain peptic ulcers in which a sizeable artery is often eroded in a crater which is semirigid as the result of the infiltration of the wall of the ulcer with scar tissue. Unfortunately there appeared to be no way of reproducing severe hemorrhage from a peptic ulcer in the experimental animal.

As aluminum hydroxide is insoluble in water, it would have no opportunity to affect the coagulability of the blood until extravasation had occurred. Presumably clotting to be effective in stopping hemorrhage from an artery would have to occur in the lumen of the vessel. Especially would this appear to be the case with an eroded artery in an ulcer where there would be little, if any, possibility for retraction to occur.

*A supply of this diet was sent to us by E. R. Squibb & Sons, New York, through the courtesy of Dr. S. Ansbacher and Dr. George Harrop.

CONCLUSIONS

Two commercial preparations of colloidal aluminum hydroxide recommended in the treatment of peptic ulcer were found to be capable of completely inactivating prothrombin in human and dog plasma.

Bleeding time from skin incisions treated with these preparations was longer than in the case of similar skin incisions treated with physiologic saline solution. The difference, however, was not statistically significant.

The bleeding time from incisions in the jejunal mucosa was not influenced by the aluminum hydroxide preparations.

It was found that one of these preparations did not destroy the vitamin K activity of cerophyl nor of 2-methyl-1, 4-naphthoquinone.

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PERITONEOSCOPY

An Analysis of 150 Cases

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VISUAL examination of the contents of the peritoneal cavity with an endoscope has become a popular diagnostic procedure during the past few years. This revived interest has been occasioned by Ruddock's[1] description of a new peritoneoscopic instrument. Recent reports in the literature have been encouraging without exception. That the peritoneoscope is highly beneficial in a number of conditions has been well established; however, it is feared the impression might be created that peritoneoscopy is advocated for the diagnosis of any and all intra-abdominal lesions. Such a misconception would serve only to bring the procedure into disfavor unjustly. Peritoneoscopy is a satisfactory procedure in selected cases, but, if used indiscriminately, the results will be disappointing.

This paper has for its purpose the critical study of 150 cases of peritoneoscopy in an effort to outline definite indications for the procedure and to call attention to the cases in which this type of examination has been of considerable assistance. On the other hand there is the desire to emphasize the visually inaccessible pathologic conditions in which instances peritoneoscopy would be a useless procedure.

Kelling[2] receives credit as the first to study the peritoneal cavity with a visual instrument. He used a cystoscope for the purpose in 1901, his first subject being a dog. Tedesko,[3] Stolkind,[4] and Roccavilla[5] later utilized various instruments for examination of the peritoneal cavity. In Chicago, Orndoff[6] reported the recognition of intra-abdominal lesions with a visual instrument in 1920. Ruddock,[1] in 1937, described the peritoneoscope and biopsy forceps which are in popular use today. Thieme,[7] in 1939, published fifty cases in detail. In 1939, Benedict,[8] Spangler,[9] Sawyer,[10] and Olim[11] also reported satisfactory results with peritoneoscopy.

TECHNIQUE

The technical steps in the procedure are quite simple.

Proper interpretation of the findings, however, requires some experience, as would be expected. After a few examinations the observer acquaints himself with the lens system and his findings become more dependable.

No unusual preoperative preparation is necessary for the examination. Morphine is given forty-five minutes previously and combined with scopolamine when disorientation is desired in a nervous patient.

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Breakfast is withheld to prevent a distended stomach from interfering with vision and care is taken to have the bladder empty before sending the patient to the operating room.

Local infiltration with novocain is used in all cases except infants and children when general anesthesia must be employed. A small stab incision is made just below the umbilicus in the average case, although the site of the incision may be varied, depending upon the presence of subumbilical scars or large masses. A nick in the anterior rectus fascia

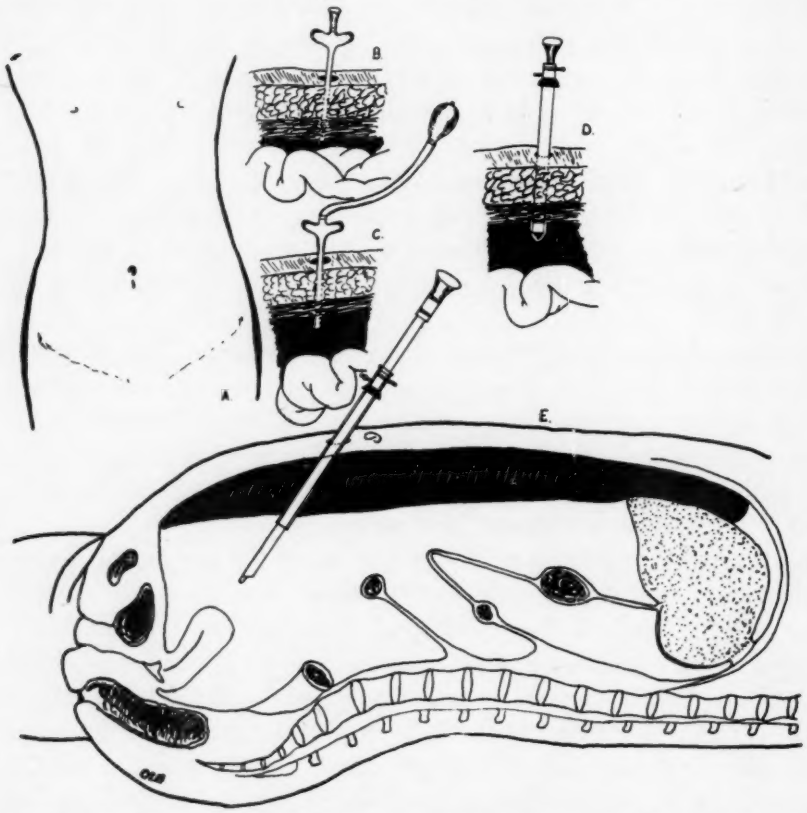

Fig. 1.—Technique of peritoneoscopy. *A*, Usual location of stab incision; *B*, introduction of pneumoperitoneum needle; *C*, pneumoperitoneum produced with atmospheric air; *D*, trocar introduced; *E*, telescope in position for viewing pelvic organs.

facilitates passage of the pneumoperitoneum needle, the peritoneum itself offering practically no resistance. Pneumoperitoneum is created with atmospheric air introduced by an ordinary hand bulb. At this point the needle may be moved about gently to determine the presence of adhesions as a guide for later passage of the trocar. No attempt is made to measure the amount of air introduced, as the quantity varies greatly depending upon the size of the abdomen, the presence of ascites, or large masses. When a moderate pneumoperitoneum exists, the trocar is inserted at an angle to either side of the vertebral column in order to prevent injury of an intestinal loop against that bony structure.

After removal of the obturator the telescope is inserted and the examination begun. The examination should proceed in an orderly fashion whenever possible. A satisfactory routine is to begin in the right upper abdomen with visualization of the right lobe of the liver and gall bladder, proceeding then to encircle the peritoneal cavity clockwise returning to the original starting point. Following this preliminary inspection attention may be concentrated upon the area of suspected pathology.

When masses are present, palpation can be combined with visualization by simply releasing air from the peritoneal cavity until the mass becomes palpable. It is possible to determine mobility of a mass with this method and, by observing the degree of indentation of the examining fingers, to learn whether the mass in question is solid or cystic. Change in position of the patient enables the examiner to increase his scope of visibility. Trendelenburg's position combined with pelvic manipulation by an assistant will usually serve to bring prolapsed pelvic organs into view. Fowler's position permits the liver to drop downward and aids in inspection of the upper surface of the liver and the diaphragm. With the patient lying on his right side the air will gravitate to the left upper abdomen and the small spleen will drop into view. The enlarged spleen can be seen easily when the patient is in a supine position.

The Ruddock biopsy forceps is an ingenious addendum. A small telescope in the forceps permits the taking of biopsies under direct vision and the tip of the instrument serves as the coagulating medium. It is possible to secure the biopsy and thoroughly coagulate the denuded area immediately, as insulation in the coagulating tip prevents charring of the specimen.

At the completion of the examination the telescope is withdrawn and the air is evacuated. Following this the sheath is removed and the skin edges approximated with one or two clips. No attempt need be made to close the deeper tissues except in infants, when one suture is advisable due to the thinness of the abdominal wall. Postoperatively the patient should be kept in bed for twenty-four hours after which time he may resume his activities.

SELECTION OF CASES

The proper selection of cases is an important phase of peritoneoscopy. Only those organs lying superficially within the peritoneal cavity are suitable for visualization. Roughly speaking, peritoneoscopy will permit the observer to see just as much of the abdominal contents as would be possible with the naked eye if the entire anterior abdominal wall were absent, plus those organs brought into view through changes in position of the body. Fig. 2 classifies diseases according to their ease of diagnosis by peritoneoscopy.

Cirrhosis of the Liver.—The liver lends itself well to peritoneoscopy. After a reasonable amount of experience any deviation from normal in the liver may be readily recognized.

Cirrhosis of the liver presents an unmistakable picture. The hobnail variety can be recognized at a glance, while early cirrhotic changes may be safely predicted by the experienced observer. It has been enlightening to discover a high percentage of cirrhotic livers in patients with deep jaundice, since jaundice is ordinarily not emphasized in medical textbooks as a prominent symptom of the disease. Peritoneoscopy is indicated in all questionable cases of cirrhosis, chiefly as an aid to prognosis.

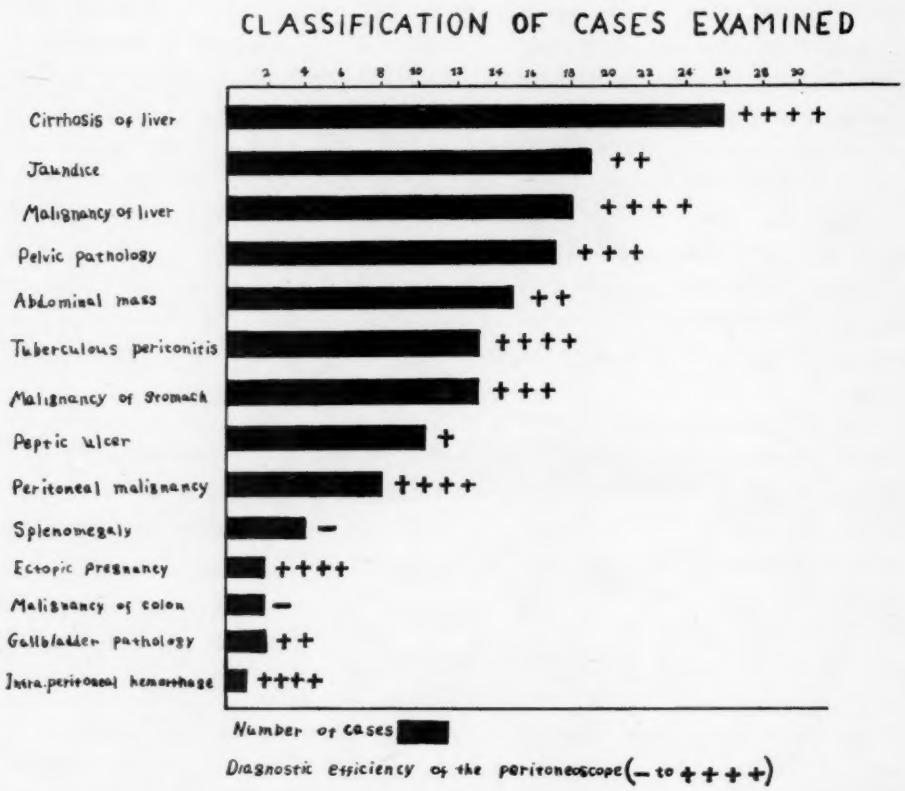
CLASSIFICATION OF CASES EXAMINED
2 4 6 8 10 12 14 16 18 20 22 24 26 28 30
Cirrhosis of liver ++++
Jaundice ++
Malignancy of liver ++++
Pelvic pathology +++
Abdominal mass ++
Tuberculous peritonitis ++++
Malignancy of stomach +++
Peptic ulcer +
Peritoneal malignancy ++++
Splenomegaly –
Ectopic pregnancy ++++
Malignancy of colon –
Gallbladder pathology ++
Intra-peritoneal hemorrhage ++++
Number of cases
Diagnostic efficiency of the peritoneoscope (– to ++++)

Fig. 2.—The cases examined comprise fourteen different pathologic conditions. Cirrhosis of the liver was the most common pathology seen with a total of twenty-six cases. Splenomegaly and malignancy of the colon are not considered indications for peritoneoscopy. The other types of pathology are classified from a 1 plus to a 4 plus, depending upon the ability to diagnose peritoneoscopically.

It will be noted in Fig. 2 that there were twenty-six cases of cirrhosis examined, the largest group of cases in the series. Because of the gratifying results, a four-plus efficiency has been awarded the peritoneoscope for this condition.

Malignancy of the Liver.—Suspicious malignancy of the liver is likewise a prime indication for peritoneoscopy. The picture is typical and easily recognized. The diagnosis is usually so definite that it is unnecessary to resort to biopsy. By shifting the patient's body it is possible to examine carefully the surfaces of the liver so that the smallest superficial nodule may be seen. Frequently the clinical differentiation be-

tween cirrhosis of the liver and malignancy is difficult. The prognosis in the two cases may differ considerably. Neither is surgical. Peritoneoscopy offers a satisfactory solution of the diagnosis.

Jaundice.—Jaundice alone is not sufficient indication for peritoneoscopy. Acute catarrhal jaundice in the young adult reveals nothing unusual other than a smooth, jaundiced liver and bile-stained organs. In a case of obstructive jaundice the peritoneoscope may show a distended thin-walled gall bladder as presumptive evidence of carcinoma of the head of the pancreas or a thick-walled contracted gall bladder which will shift the evidence toward a diagnosis of common duct stone. In either condition, however, the peritoneoscope does not reveal the complete picture, as it is impossible in most cases to visualize the pancreas or the common duct. This type of case should be considered surgical in order that the patient can receive the benefit of exploratory laparotomy. Jaundice cases warrant a peritoneoscopic examination only when additional symptoms indicate possible malignancy of the liver, gall bladder, or a cirrhosis of the liver.

Tuberculous Peritonitis.—The peritoneoscope has one of its greatest fields of usefulness in this condition. The diagnosis may be readily made in most cases and in the occasional case of peritoneal carcinomatosis, when the differentiation is confusing, a biopsy will clarify the diagnosis.

The pneumoperitoneum was purposely undisturbed in all cases on completion of the examinations. Two of the thirteen cases appeared to receive some benefit from the retained air as shown by diminished temperatures, although the remaining eleven cases revealed no changes.

Peritoneal Malignancy.—There were eight cases of peritoneal carcinomatosis in this series, all revealing typical findings. The peritoneoscope offers a high degree of accuracy in these cases. If any question exists, a biopsy may be taken without hesitation because of the relative avascularity of the peritoneum.

Ectopic Pregnancy.—Two cases of ectopic pregnancy were observed, both being ruptured tubal pregnancies. Of all the peritoneoscopic examinations performed, none were more satisfactory from a diagnostic standpoint than these two cases. Free blood was conspicuous in the peritoneal cavity and visualization of the pelvis in Trendelenburg's position showed the point of tubal rupture in each instance. Most cases of ectopic pregnancy are obvious. Peritoneoscopy, however, will be of service in cases of rupture when the diagnosis is questionable. Nonruptured ectopic pregnancies may sometimes be indistinguishable from uterine pregnancies. The Aschheim-Zondek test would be of no value in these cases. Peritoneoscopy should solve the problem without disturbing an existing uterine pregnancy.

Intraperitoneal Hemorrhage.—Suspicious hemorrhage can be detected promptly with the peritoneoscope. One case of possible spontaneous hemorrhage was examined and the peritoneal cavity was found to be

filled with blood. Operation later revealed a varix of the omentum which had ruptured. Coleman[12] reports the use of a small trocar to determine the presence of intraperitoneal hemorrhage. A slightly larger trocar may be used, however, to accommodate the peritoneoscope with the added advantage of visualization in those cases where no greatly increased intra-abdominal pressure exists to force the blood out through a trocar.

There is a place for peritoneoscopy in cases of possible intra-abdominal hemorrhage without external evidence of injury. Such patients, frequently the victims of automobile accidents, have head injuries which serve to confuse the picture. The peritoneoscope may prevent unnecessary laparotomies in this type of critically ill patients.

Malignancy of the Stomach.—There were twelve cases of malignancy of the stomach. One case was diagnosed peritoneoscopically as sarcoma with a confirmatory biopsy. An additional case in which no tumor could be seen with the peritoneoscope proved to be a gastric ulcer at operation. Only those lesions involving the anterior wall of the stomach can be seen. In the obese type of individual the stomach is often completely obscured by the liver; nevertheless, a little practice enables the examiner to elevate the liver with the tip of the instrument and to study the stomach at close range. Distention of the stomach by an indwelling nasal catheter will usually roll that organ out into view.

It is the status of the malignancy on the posterior wall, however, that cannot be determined with the peritoneoscope. It is impossible to learn whether the lesion has penetrated into the pancreas or not. Because of this deficiency only a three-plus accuracy is awarded the peritoneoscope in diagnosis of malignancy of the stomach. (Fig. 2.) In spite of the admitted inadequacy of the peritoneoscope, the results in this series of cases suggest that all carcinomas of the stomach be routinely peritoneoscoped. This measure is not aimed at diagnosis of the lesion in the stomach per se, as roentgenographic study is more capable of such, but rather at the determination of operability of the case.

It is generally agreed that metastases to the liver and peritoneum render a patient inoperable with the exception of palliative surgery in the obstructive type of lesion when a gastroenterostomy will give temporary relief. In this series of eleven cases of carcinoma of the stomach, four had liver metastases, while two others were considered inoperable because of marked local extension into the peritoneum and adjacent organs. Of these latter two cases one died three weeks later of cachexia. Hence six, or 54 per cent, of these cases were grossly inoperable and were saved from needless surgery by the peritoneoscopic examination. (Fig. 3.) Of the five cases recommended for surgery, one was considered clinically inoperable because of palpable abdominal masses thought to be peritoneal metastases. On peritoneoscopy these masses were discovered to be epigastric hernias. At operation this patient was found to

have a resectable lesion. The four remaining patients recommended for laparotomy because of absent visible metastases all had lesions involving the pancreas and were nonresectable.

Peritoneoscopy will prevent unnecessary surgery in a fair proportion of cases of carcinoma of the stomach. Those patients without visible metastases and obvious local involvement will not be jeopardized, as laparotomy can be done to determine operability definitely.

Peptic Ulcer.—The peritoneoscope was used in eleven cases of suspected peptic ulcer, two of which were possible perforations. Practically all of these examinations were carried out during the earlier experience with the instrument.

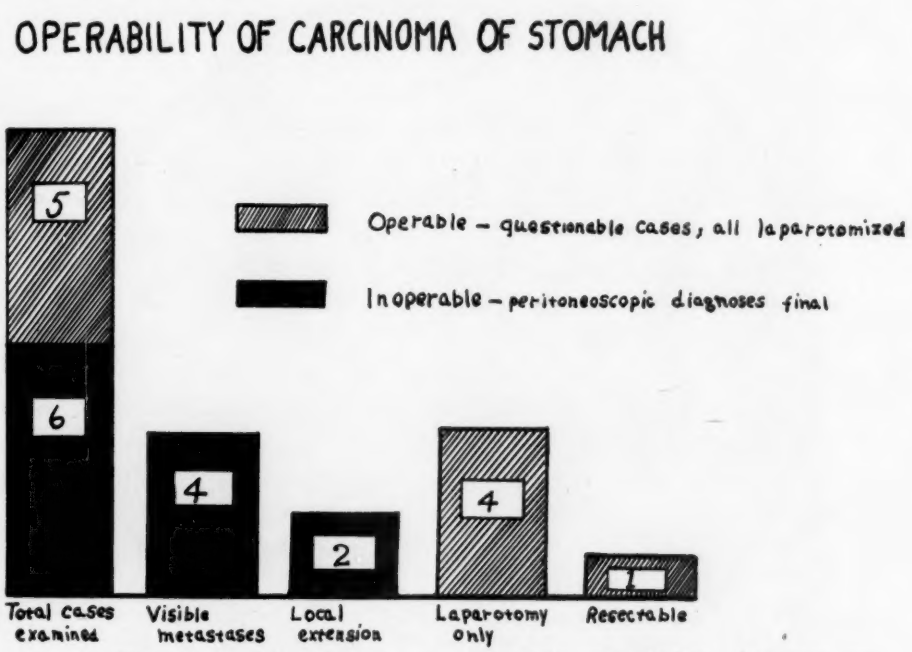

Fig. 3.—Eleven cases of carcinoma of the stomach were studied. Six were considered inoperable, while only five were recommended for laparotomy after peritoneoscopic examination.

Insignificant serosal changes accompanying an ulcer of the stomach may be overlooked with the peritoneoscope. The duodenum cannot be visualized in a sufficient number of cases to make the procedure trustworthy. Both roentgenographic examination and the gastroscope have far more diagnostic value in these cases. The use of the peritoneoscope may be reserved for the small group of cases in which an ulcer perforation is so atypical that there is hesitation of laparotomy, yet the fear exists of allowing the optimal time of operation to pass.

Pelvic Pathology.—Visualization of the pelvic organs can usually be carried out with a high degree of success, particularly when combined with manipulation per vagina. Questionable ectopic pregnancy has been discussed previously as an important indication. Ovarian or uterine tumors lend themselves well to inspection. Biopsies of such tumors are of material assistance and may be taken readily in the average case.

Pelvic inflammatory disease, however, may offer difficulties to the examiner and it is because of this condition that a three-plus efficiency is allotted in Fig. 2. Both recent and old pelvic inflammatory processes frequently result in adhesions between the pelvic organs with obliteration of landmarks so that it may be impossible to classify distinctly the status of the organs. A tubo-ovarian abscess may be fused with the uterus so that normal boundaries are indistinct. The surgeon will appreciate this situation, as the same difficulty often exists at laparotomy and blunt dissection must be carried out before the adherent organs are mobilized sufficiently for identification to be made.

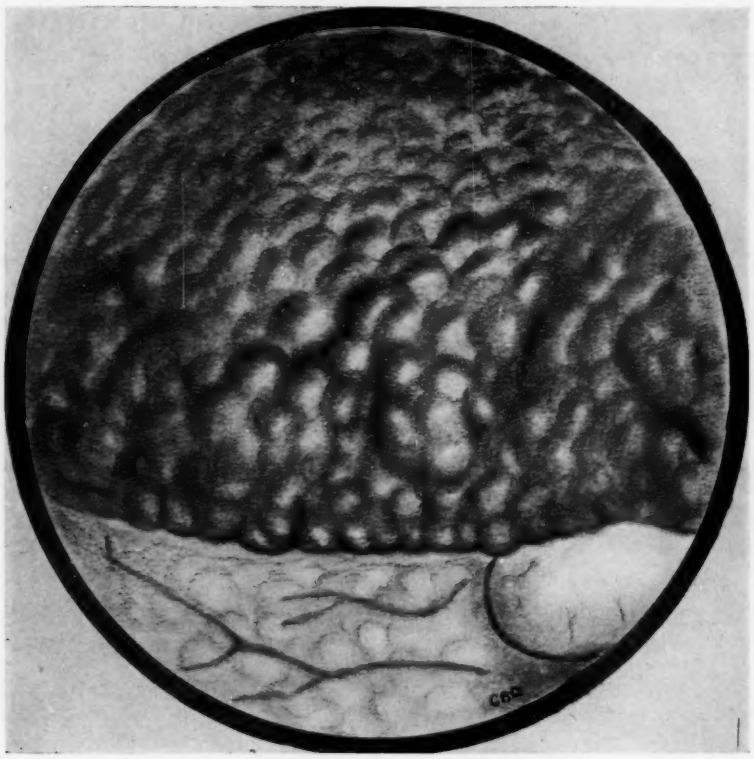

Fig. 4.—Advanced hobnail cirrhosis of the liver as seen through the peritoneoscope.

Abdominal Masses.—If the abdominal mass lies superficially in the peritoneal cavity, its diagnosis may be simple and spectacular. If covered by omentum, intestines, or other organs, it may be impossible to arrive at a definite diagnosis. Hydrops of the gall bladder, cysts or tumors of the liver, tumors of the stomach, and masses arising from the pelvis are easily differentiated. A large cyst almost filling the peritoneal cavity will be noted as such, but the likelihood of determining its origin will be slight unless the cyst can be moved about with change in position of the body. Retroperitoneal tumors can only be diagnosed as such, although in one instance the diagnosis of tumor of the right adrenal gland was made while totally unsuspected clinically, and operation verified the peritoneoscopic findings.

Peritoneoscopy should be used for abdominal masses when clinical diagnostic measures have failed, bearing in mind that the instrument will offer little or no assistance unless the mass is superficially placed.

Gall Bladder Pathology.—Because of its exposed position the gall bladder offers no obstacles to visualization. The normal robin's egg-blue color is distinct and any variations are easily noted. Acute cholecystitis gives an unmistakable picture. Malignancy of the fundus may be recognized without difficulty.

In many instances, however, examination of the gall bladder is not complete or dependable unless the extrahepatic bile ducts can be examined also for pathology. The peritoneoscope cannot visualize the biliary duct system and hence this examination is not recommended for cases in which such pathology is likely. If interest centers on the gall bladder alone, peritoneoscopy will be entirely satisfactory.

Fig. 5.—Carcinoma of the stomach with serosal involvement viewed through the peritoneoscope.

No gallstones have been palpated with the tip of the instrument as described by Steiner;[13] nevertheless, it should be easy to palpate a large barrel-shaped stone in a contracted gall bladder that was partially empty of bile. Small stones floating in bile obviously would be difficult to palpate.

Splenomegaly.—The enlarged spleen is easily seen with the peritoneoscope. The small spleen is brought into view by placing the patient on his right side.

In Fig. 2 it will be noted that splenomegaly is not considered now as an indication for peritoneoscopy. Splenomegaly itself is diagnosed by abdominal palpation. Visualization of the spleen, although easily accomplished, is usually disappointing because of the difficulty in interpreting gross appearances. No aid is to be had from the microscope, as biopsy of that organ is too hazardous for safety. Blood studies and the clinical history will usually give decidedly more information about a splenomegaly than the peritoneoscope can offer.

Fig. 6.—Ruptured right tubal pregnancy, peritoneoscopic view. Note the large clot adherent at the site of rupture.

Malignancy of the Colon.—The peritoneoscope should be used only for the determination of operability of malignancy of the colon in cases where liver metastases are suspected. Neither the colon nor small intestine is accessible in a sufficient number of cases to make the procedure dependable. The loop of intestine containing the pathology might be obscured by other loops with the result that the diagnosis will be missed.

Appendicitis and Peritonitis.—In view of the fact that the appendix is retrocecal in the majority of cases it is no wonder that it is rarely seen. These observations on the accessibility of the appendix have been made in cases with other than appendical pathology in which the appendix has been searched for as a routine measure. Peritoneoscopy is definitely contraindicated in suspected cases of acute appendicitis.

Acute peritonitis from any cause should be avoided. The possibility of activating such an infection is great and there is the increased danger

of intestinal perforation due to adhesions between the visceral and parietal peritoneum.

ACCURACY OF PERITONEOSCOPY

A follow-up of patients reveals that the diagnoses have been proved in 44 of the total 150 cases. The final diagnoses have been made by either autopsy, operation, or biopsy. These 44 cases have been utilized as a check against the accuracy of both clinical and peritoneoscopic diagnosis. Fig. 7 contains these statistics.

Of the 44 diagnoses substantiated, the clinical diagnosis was correct in 24 cases, giving a clinical accuracy of 54.5 per cent. The peritoneoscopic diagnosis was found to be correct in 40 of the cases, with an accuracy of 90.9 per cent. These statistics compare rather closely with those compiled by Ruddock.[1] The peritoneoscopic accuracy should remain consistently high if there is a proper selection of the cases to be examined.

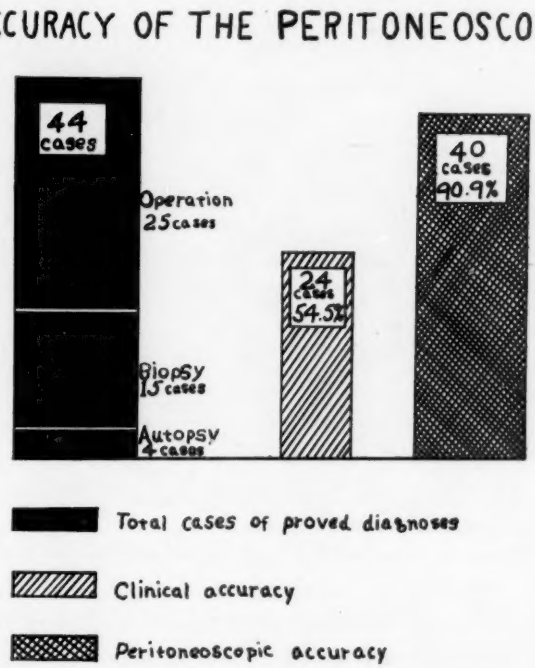

Fig. 7.—There were forty-four cases with diagnoses proved by either operation, biopsy, or autopsy. The accuracy of both clinical and peritoneoscopic diagnoses is shown.

The four peritoneoscopic errors consist of: (1) diagnosis of ovarian cyst proved at operation to be a tubo-ovarian abscess; (2) failure to recognize an acute yellow atrophy of the liver in a young male, diagnosis clarified by autopsy; the peculiar splotching of the liver was described at peritoneoscopy, but its true significance was not appreciated; (3) peritoneoscopic diagnosis of abdominal Hodgkin's disease which at autopsy proved to be a metastatic carcinoma; (4) inability to determine the nature of a deeply situated abdominal mass; operation revealed the mass to be carcinoma of the mesentery.

A glance at these so-called peritoneoscopic errors will reveal that the first three are actually personal errors, failures to recognize visible pathology, while only the last one is a true mechanical error, attributed to an inability to bring the pathology into view.

ACCIDENTS AND COMPLICATIONS

There were three accidents in this series of cases (Table I). The two nonfatal accidents were intestinal perforations, in one with the pneumoperitoneum needle, in the other with the trocar. No operation was done in either case.

TABLE I

ACCIDENTS AND COMPLICATIONS

PERITONEOSCOPIC DIAGNOSIS	ACCIDENT	RECOVERED	DIED
None (Clinical, peritoneal carcinomatosis)	Pneumoperitoneum needle introduced into intestine; paracentesis 2 days previously	No operation; no evidence of peritonitis	
None (Clinical, tuberculous peritonitis)	Trocar entered intestine	No operation; recovered without peritonitis or wound infection	
(Abdominal, Hodgkin's disease)	Perforation of small cholangitic abscess with biopsy forceps while attempting biopsy of liver nodule; accident recognized but, in view of widespread metastases and poor condition, operation thought unwise		Died 7 days later; autopsy: bile peritonitis, carcinoma of head of pancreas with metastases to peritoneal cavity and mediastinum

RESULTS

	CASES	MORTALITY RATE
Total cases examined	150	
Accidents	3	
Deaths	1	0.6%

Because of the ease with which the instruments perforated the intestines just as the peritoneum was entered, it was concluded that the involved loops were firmly adherent at the points of perforation and that the general peritoneal cavity would not be soiled. Both patients were observed very carefully for signs of beginning peritonitis, but none appeared. Their recoveries were uneventful without even a wound infection in either case.

Many observers have noted that nonadherent intestinal loops will slip away from the trocar. Kelling[14] called attention to this phenomenon. Ruddock[1] reported bowel perforation in eight of his cases, all of them being operated upon shortly afterward. He found that, in view of dense adhesions between the perforated intestines and the parietal peritoneum, no peritoneal soiling would have occurred in any of the cases.

The decision as to whether or not to explore following the perforation of an intestine should depend upon circumstances surrounding the case.

Evidence points toward the safety of close observation without immediate laparotomy in those cases where adhesions are suspected due to the superficial position of the involved intestine. If there exists considerable doubt in the examiner's mind of sufficient mechanical protection for the site of perforation, then immediate laparotomy should be performed.

The one fatal accident was caused by an error on the part of the examiner. The patient with a known mediastinal tumor was found to have multiple abdominal masses on peritoneoscopy. An attempt was made to secure a biopsy of an apparent liver nodule with the result that a cholangitic abscess wall was perforated. Care in palpation of the mass in the liver with the tip of the instrument would have shown its true cystic nature and prevented the accident. Bile was seen to escape from the perforation, but, in view of the patient's widespread malignancy and poor condition, operation was decided against.

There have been but few additional complications with the peritoneoscope. Occasional cases of mild subcutaneous emphysema have been noted, but all subsided rather promptly. There were no hernias, wound infections, or hematomas in the series. There was only one instance of shoulder pain from pneumoperitoneum, which occurred in a patient with a ruptured tubal pregnancy. She complained of right shoulder pain shortly after inflation of the peritoneal cavity was begun. It is interesting to observe that the peritoneal cavity may be inflated to its maximum without the production of shoulder pain, while many cases of such pain are reported following the injection of much smaller quantities of air during tubal patency tests. Even extreme Fowler's position in greatly inflated cases has not been productive of shoulder discomfort. No explanation is offered for the apparent paradox.

SUMMARY AND CONCLUSIONS

1. The present report is based on 150 personal cases of peritoneoscopy. Statistics are presented in an effort to aid in the selection of cases suitable for this type of examination.

2. The technique of examination is described. The procedure is essentially the creation of a pneumoperitoneum followed by the introduction of a telescope which permits the observer to view the peritoneal cavity and its superficial organs in detail with a clear undistorted vision.

3. Biopsies of organs in the peritoneal cavity may be taken with safety by the use of a special telescopic forceps developed by Ruddock.

4. Emphasis has been placed on the selection of cases. Only those organs which either lie superficially in the peritoneal cavity or may be brought into a superficial location by change in position of the body or by manipulation are amenable to visualization. Failure to consider these facts will usually be productive of disappointing results.

5. The conditions affording the most satisfactory results with peritoneoscopy may be listed as follows: cirrhosis of the liver, malignancy of the liver, tuberculous peritonitis, peritoneal malignancy, ectopic pregnancy, intraperitoneal hemorrhage, pelvic pathology, and the determination of operability of malignancy of the stomach.

6. An analysis is made of 44 cases in which the diagnosis was proved by either operation, biopsy, or autopsy. In this group the clinical diagnosis was accurate in 54.5 per cent of the cases while a 90.9 per cent accuracy was obtained with the peritoneoscope.

7. There were 3 accidents in the series of 150 cases, only 1 of which was fatal, giving a mortality of 0.6 per cent. It should be considered that a large number of the patients examined were bad risk cases that were subjected to peritoneoscopy with the hope that laparotomy could be avoided if possible.

8. In comparison with laparotomy, peritoneoscopy is a minor operative procedure with very little discomfort to the patient and economically important in that it requires only one day of hospitalization, following which the patient may become ambulatory.

9. Peritoneoscopy has proved to be a valuable adjunct in diagnosis. It is not a fad but rather a procedure which has definite indications and limitations. The peritoneoscope will not supplant laparotomy but will render operation unnecessary in many cases. On the other hand, following peritoneoscopy a number of cases will be revealed as surgical that were not considered so beforehand.

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SELF-INTRODUCED FOREIGN BODY PERFORATING LARGE BOWEL

Operation with Recovery

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FOREIGN bodies in the large bowel have been reported by Branning, Pamperi, Neese, Koucky and Beck, and many others. These cases are always interesting and instructive. The case I am reporting presents a few unusual features which will be discussed.

Fig. 1.—Roentgen ray disclosing screwdriver in region of splenic flexure.

Case Report.—N. J. (No. 19956), a 35-year-old colored male, entered the Cook County Hospital on April 8, 1940, stating that during the preceding week he had developed a tender swelling in the left inguinal region which extended into the scrotum. He had had a small "lump" on the left side since he was 2 years old and he had always been able to push the "lump" back until recently, when it had become "big and sore." He further stated that he also had a "falling of the intestines" (prolapsed rectum). His rectal prolapse became excessive seven days prior to his admission to the hospital while he was carrying wood. To replace his prolapsed rectum, he went to his shack and procured an 8-inch screwdriver which he placed, handle first, into his anal orifice. The prolapse was relieved. Much to his surprise, he lost control of the screwdriver and it too disappeared. He attempted to extract it, first with his fingers and then with a soupspoon. These attempts having failed, he desisted from further effort. It was at this time (seven days

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before his entrance) that his inguinal hernia became irreducible. He managed to hitchhike his way to Chicago, a distance of about 400 miles. During this four-day trip he noticed that he still could not reposit the inguinal hernia, although he experienced no discomfort. A day after his arrival in Chicago his scrotal mass and inguinal region became painful and tender. The pain was not severe but was aggravated by walking and coughing. During the ensuing two days the mass became more painful and he thought he should have a doctor see it. He did not vomit and he had his last bowel movement two days before entering the hospital.

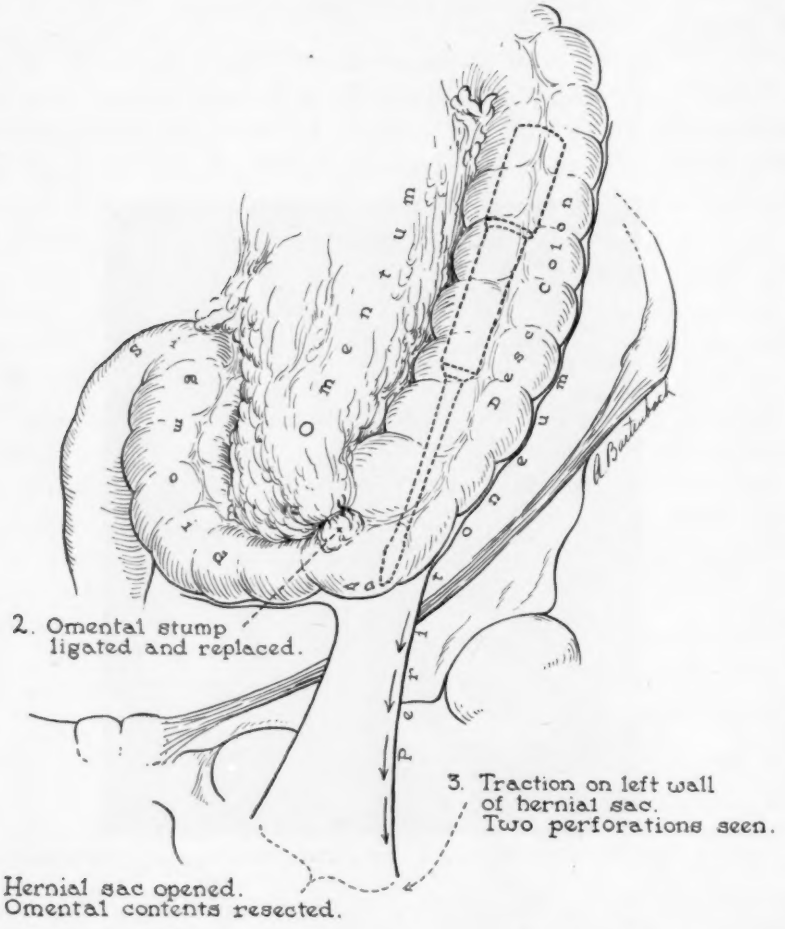
Omentum
Descending Colon
Stomach
Peritoneum
2. Omental stump ligated and replaced.
3. Traction on left wall of hernial sac. Two perforations seen.
1. Hernial sac opened. Omental contents resected.

Fig. 2.—Steps of operation diagrammatically outlined.

His past history revealed that he had had a right herniorrhaphy five years before, gonorrhea several times, and had been treated for syphilis in 1926. Physical examination revealed a well-developed and well-nourished colored male who did not appear acutely ill. His temperature was 100.2° F.; his pulse, 80; and respirations, 20 per minute. His blood pressure was 100/82. The abdomen was flat (umbilicus on the xiphopubic line). Tenderness was present over the left upper and lower quadrants. The patient stated that he could feel the screwdriver in his left upper quadrant, but this could not be verified by the examining physicians. No masses were palpable. Peristaltic sounds were present but diminished (six to eight per minute). The sounds were not those of obstructive borborygmi but resembled normal clicks and gurgles. The left inguinal region presented a mass which extended

into the scrotum. It was very tender, irreducible, and did not transilluminate. Rectal examination revealed no prolapse or hemorrhoids, hence this phase of his story was doubted. No masses or foreign bodies could be felt.

The patient was subjected to fluoroscopy and x-ray examination revealed a screwdriver, the handle of which lay in the region of the splenic flexure (Fig. 1). The jagged end of the tool lay near the junction of the descending colon and sigmoid.

The patient was given a morphine-scopolamine sedative followed by a local infiltration with novocain in the inguinal region. He developed a scopolamine "jag" and became so uncooperative that nitrous oxide anesthesia was resorted to. A left inguinal incision was made and the aponeurosis of the external oblique muscle was divided. The hernial sac and spermatic cord were delivered. On opening the sac, free serous fluid gushed out. The omentum was firmly attached to the lateral wall of the sac which necessitated its being cut between two hemostats and then ligated. The omentum, freed from its distal attachment, was inspected and found to be very hard and fibrotic. This indurated area, measuring 29 by 24 cm., was resected. The omental stump was replaced into the peritoneal cavity (Fig. 2).

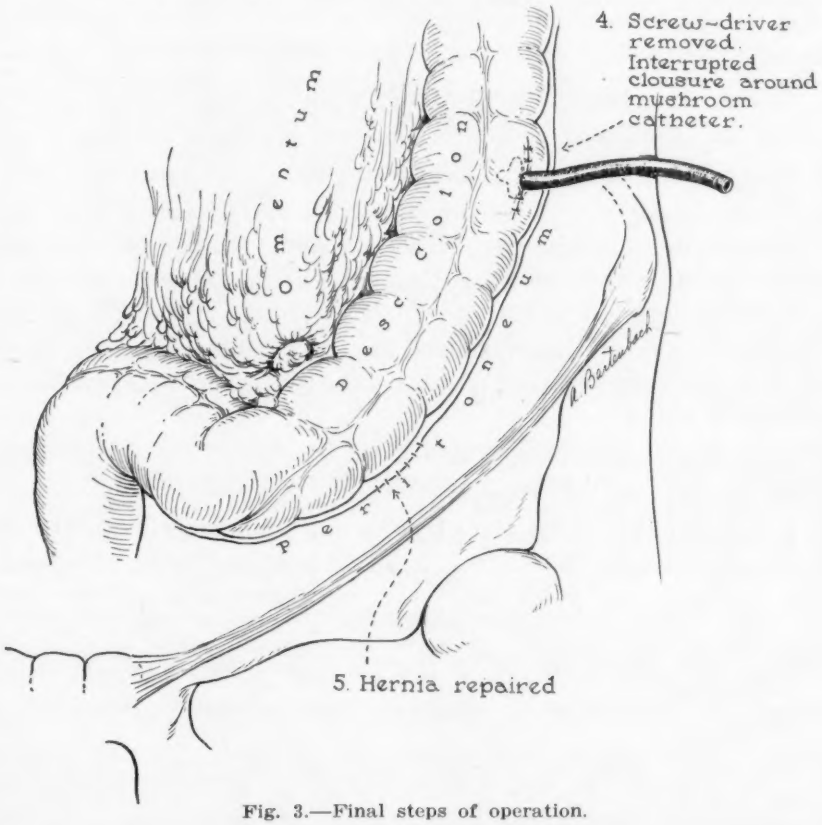

Fig. 3.—Final steps of operation.

Traction was made on the hernial sac and the sigmoid was found to be attached to the lateral sac wall. The diagnosis of a sliding hernia was made. The tip of the screwdriver could now be felt. Two perforations were found in the sigmoid in the region occupied by the jagged tip of the screwdriver. An opening was made in the bowel, beginning at the sigmoid perforations and extending about 2 inches cephalad into the descending colon. This incision connected both perforations, converting these into one opening. Through this opening the screwdriver was delivered. A de Pezzer catheter was placed into the defect which was closed by

interrupted through-and-through catgut sutures around the catheter. One of these sutures was passed through the catheter to anchor it to the bowel wall. No second layer of sutures was placed because of fear of tension. A stab wound was made in the left loin and the catheter pulled through this. The hernial sac was then ligated distal to the sigmoid attachment. A modified Bassini repair with interrupted catgut sutures completed the operation. (Fig. 3.) One cigarette drain was placed subcutaneously.

For two days following the operation the patient's rectal temperature mounted to 103.8° F. The pulse also reached its maximum of 120 during these two days. Following this the temperature and pulse steadily dropped until the eighth postoperative day when normal levels were reached and maintained. His convalescence was quite uneventful. The mushroom catheter was removed on the seventh postoperative day. The colostomy site stopped draining on the twentieth day. He received by transfusion 1,000 c.c. of citrated blood and 100 c.c. of 0.8 per cent sulfanilamide solution subcutaneously. He was kept on intravenous dextrose and saline solution for the first three postoperative days. He was discharged in good condition twenty-two days following the operation.

SUMMARY AND COMMENT

1. A case of a large, sharp, foreign body, self-introduced and perforating the bowel with soiling of the peritoneum, is reported.

2. The foreign body was removed surgically and recovery resulted.

3. While throughout the entire procedure the operative field, intra- and extraperitoneal, was grossly contaminated with feces and while the only drainage used was a rubber tube in the large bowel and one subcutaneous cigarette drain and no attempt was made to cleanse the peritoneal cavity, infection remained localized. Whether or not the two small bowel perforations created some sort of intraperitoneal vaccination remains *sub judice.*

4. Abdominal auscultation aided in suspicion of intraperitoneal damage because the intestinal sounds were definitely diminished.

5. Retroperistalsis obviously played a part in determining the final position of the foreign body since the handle abutted the splenic flexure.

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EXCISION AND/OR PROXIMAL LIGATION OF EXTRAOSSEOUS THROMBOPHLEBITIS IN THE TREATMENT OF ACUTE HEMATOGENOUS OSTEOMYELITIS WITH POSITIVE BLOOD CULTURE

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THE following case is reported (1) because it demonstrated particularly well the thrombophlebitic nature of the local bone lesion of acute hematogenous osteomyelitis; (2) because it demonstrated the relationship of the bacteriemia to the local bone lesion; (3) because it showed marked similarity to cases of mastoid disease with jugular vein thrombosis; (4) because the thrombophlebitis made an important indication for treatment; and (5) because it demonstrated the necessity for looking for similar accessible thrombophlebitis in all other cases of acute hematogenous osteomyelitis with bacteriemia with the idea of excision or proximal ligation of such affected veins draining the bone focus in order to control the general infection.

CASE REPORT

(Doctor's Hospital, No. 25649, Feb. 22 to March 9, 1940.) In a boy 12 years of age with a negative family history and a previous history of a pneumococcus meningitis at the age of 2 years with recovery except for a residual bilateral complete deafness a small infection of the right big toe (paronychia) was followed by a focus of osteomyelitis in the upper end of the left tibia. At the time of admission to the hospital, the patient was markedly toxic, had a high temperature, and was stuporous.

The bacteriologic studies showed a *Staphylococcus aureus* bacteriemia of the magnitude of 12 colonies per cubic centimeter of blood cultured. The patient was put on an adequate dosage of sulfanilamide and, later, sulfathiazole. However, there was no effect of the chemotherapy upon the bacteriemia, although the general condition of the patient improved somewhat, and the local condition continued unchanged. Several days after admission a thrombophlebitis of the saphenous vein was noted and the latter could be traced as extending directly from the area of the osteomyelitis in the head of the tibia upward and downward into the adjoining segment of the saphenous vein. The indication for excision of the vein seemed obvious and the similarity to cases of acute mastoiditis with jugular vein thrombosis was noted.

This was confirmed at the operation. There was a suppurative inflammation of the skin and subcutaneous tissue over the inner condyle of the tibia; the thrombophlebitis of the saphenous vein originated in this area which was continuous with the focus of osteomyelitis; and it was possible to dissect out and remove the entire thrombosed vein well into healthy tissue both above and below. The bone itself was not touched in any way. The wound was left wide open and packed with iodoform gauze.

The bacteriemia disappeared immediately thereafter. The local wound from which the vein had been removed healed very well and at the end of two weeks the boy was discharged from the hospital.

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The area of osteomyelitis was demonstrated roentgenographically and its progressive spontaneous defervescence, revascularization, and healing was followed and similarly demonstrated. Several very small sequestra escaped or were removed from the wound during this period after which the very small sinus closed completely. The follow-up observation period is now sixteen months.

DISCUSSION

Although the local bone lesion in acute hematogenous osteomyelitis is a secondary matter to a bacteriemia originating from a primary lesion elsewhere (in this case a paronychia of one of the opposite toes), this case demonstrates conclusively that the local lesion itself in its turn can act as a local point of distribution for a secondary bacteriemia. A suggestive clinical point is that the secondary bacteriemia is usually of small magnitude, approximately under 25 colonies of bacteria to the cubic centimeters of blood cultured.

This type of bacteriemia is not influenced at all by chemotherapy with drugs of the sulfanilimide group. A bacteriemia of small magnitude continues because the thrombophlebitis keeps discharging bacteria into the circulation.

Under these conditions, clinicians should search carefully in the nearby veins for an accessible thrombophlebitis. Should such a thrombophlebitis be found, the indication becomes absolute to excise the affected segment of vein or to ligate it on the proximal side. In the absence of such demonstrable thrombophlebitis, the question of ligating the principal vein draining the affected area should be considered with due consideration to its feasibility anatomically and to any subsequent and consequent circulatory change.

All of this concerns itself only with the control of any bacteriemia which accompanies a focus of acute hematogenous osteomyelitis. The management of the bone focus itself should follow along well-established lines. My own very conservative viewpoints regarding the management of the local bone focus has been discussed very frequently and is marked by the most extreme conservatism as the management of the above described case shows.

In a personal communication, Dr. Champ Lyons, of the Massachusetts General Hospital, tells me that he also has recognized the importance of ligating the main tributary vein of the local bone focus as one of the items in his management of acute hematogenous osteomyelitis.

MESODERMAL MIXED TUMORS OF THE CORPUS UTERI

Report of a Case With Review of the Literature

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INTRODUCTION

IT IS our purpose to describe an instance of an extremely rare tumor, the mesodermal mixed tumor of the body of the uterus. It belongs to a remarkable group of bizarre tumors which originate from cells normally absent in the uterus. After a painstaking review of the literature of mixed tumors, sarcomas of the simple and more complicated types, teratomas, lipoma, chondroma, osteoma, etc., of the cervix and corpus of the uterus, we have been able to collect only twelve genuine mesodermal tumors of the corpus acceptable by the pathologic criteria of Lawen.[1] There is much confusion in the literature concerning this tumor, and it is our object not only to establish its proper position, but also to throw light upon its nature.

The more important findings of these tumors have been classified in Table I. In the list of verified cases acceptable by the adopted diagnostic pathologic criteria described elsewhere, we have paid careful attention to the microscopic descriptions in each published case. All cases of pure rhabdomyoma or rhabdomyomosarcoma of the uterus, such as those reported by Blair Bell[2] and Glynn, Lochrane,[3] and others, were rejected. The case of Wolfe[4] has been unacceptable. His tumor apparently presented all of the clinical and pathologic characteristics of a genuine mesodermal mixed tumor. Although the bulk of the tumor consisted of "nonstriated muscle cells intermingled with myxomatous tissue, osteoid and cartilage," a careful examination of the pathologic report of his case failed to reveal any true embryonal myoblasts. The absence of striated embryonic muscle cells so necessary for a pathologic diagnosis serves to eliminate those cases described as adenosarcoma by Sophian.[5] Simple tumors, such as osteoma, chondroma, etc., have not been included in this list.

The first case in the uterus was reported by Weber[6] in 1867. The tumor sprang from the cervix uteri of a multipara, 45 years of age, and revealed the characteristic microscopic structure of a mixed tumor. The first case of the body of the uterus was described by Anderson-Edmonnson in 1870 and the second by Bysttumoff-Eckert in 1874 (quoted by Kehrer).[7]

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TABLE I

REPORTED BY	AGE	PARITY	ORIGIN, SITE, CHARACTER	MICROSCOPIC FINDINGS	SYMPTOMS AND PHYSICAL SIGNS	TREATMENT	COURSE AND TERMINATION
1. Anderson, Edmonnson, 1870. Quoted by Kehrer, E.: Monatschr. f. Geburtsh. u. Gynäk. **23**: 646, 1906.	50	None	Corpus uteri; large soft nodular tumor	Typical striated muscle; cystic glands; small mononucleated and large multinucleated cells	?	Hysterectomy	Death from hemorrhage
2. v. Franqué, O.: Ztschr. f. Geburtsh. u. Gynäk. **40**: 183, 1899.	49	Para xi	Posterior wall of fundus and body; circular tumor size of a man's head filling the uterine cavity; polypoid and reddish white in color	Embryonal muscle cells; myxomatous tissue; sarcoma cells	Pelvic pains for 2 wk. before admission; marked anemia; fundal tumor discharging pus felt through dilated cervix	Total abdominal extirpation of uterus	Death 1 wk. after operation due to peritoneal metastases
3. Läwen, A.: Beitr. z. path. Anat. u. z. allg. Path. **38**: 177, 1905.	60	?	Posterior wall of fundus of uterus; tumor about the size of a child's head; polypoid, soft, variegated brown to white in color	Embryonal striated muscle cells; glands; sarcomatous cells; hyalinized connective tissue; carcinomatous cells	Scanty postclimactic vaginal bleeding for 6 mo.; uterus on admission was not enlarged	Vaginal hysterectomy	Local recurrences and peritoneal metastases (incomplete; no autopsy); death 11 mo. after onset with clinical picture of abdominal metastases
4. Hunziker, D. H.: Beitr. z. Geburtsh. u. Gynäk. **12**: 317, 1907-08.	58	Para ii	Anterior wall of fundus; tumor mass round, polypoid, marmorated, grayish red, nodular and of very variable consistence; measurements, 6 by 4 by 5 cm.	Smooth and cross striated embryonal muscle cells; cartilage; myxomatous tissue; sarcomatous tissue; glands	Painless bloody vaginal discharge associated with increased frequency of urination 5 to 6 wk. before admission; tumor about size of male fist palpated 1 fingerbreadth above symphysis; fundus retroflexed	Total abdominal hysterectomy	Death 5 mo. after onset with local recurrences, abdominal metastases, and progressive emaciation

5. Herb, I. C.: Surg., Gynec. & Obst. **10**: 463, 1910.	55	Para iii	Fundus; polypoid tumor filling the entire uterine cavity with much enlargement of the uterus	Embryonal striated muscle cells; cysts lined by epithelial cells	Onset 8 mo. before admission with pelvic discomfort; watery and, at times, bloody vaginal discharge; emaciation; enlarged uterus; generalized pelvic tenderness	Supravaginal hysterectomy	Regional recurrences with death 6 mo. after operation
6. Nicholson, G. W.: Guy's Hosp. Rep. **69**: 173, 1918.	55	Para i	Primary multicentric, multiple mesodermal mixed tumor of body of uterus	Embryonal skeletal muscle cells; smooth muscle; fat; cartilage; myxomatous tissue; round- and spindle-celled sarcoma; carcinoma; carcinosarcoma	Six months' history of pain in chest followed by dyspnea; loss of weight; hard tumor palpable just above symphysis pubis	None	Death 9 mo. after onset with multiple metastases to left pleura, lungs, liver, ovaries, and peritoneum of Douglas' pouch
7. Chavannez, M., and Nadel, P.: Case I La Gynecologie **19**: 3, 1920.	50	None	Posterior wall of fundus; tumor the size and volume of a fetus at term; polypoid and nodular; irregular consistence; variegated color; invasion of uterine cavity and myometrium	Embryonal muscle cells; sarcoma cells; myxomatous tissue; glands; cartilage; osteoid tissue	Pelvic violent pains of 10 mo. duration; pelvic mass	Total hysterectomy	Death 15 mo. after onset; clinical evidence of generalized metastases in abdomen and disturbances of bladder

TABLE I—CONT'D

REPORTED BY	AGE	PARITY	ORIGIN, SITE, CHARACTER	MICROSCOPIC FINDINGS	SYMPTOMS AND PHYSICAL SIGNS	TREATMENT	COURSE AND TERMINATION
8. Chavannez, M., and Nadel, P.: Case II, La Gynecologie **19**: 3, 1920	59	?	Posterior wall of corpus uteri greatly enlarged; tumor of irregular consistence; extensive invasion of myometrium	Embryonal muscle cells; cartilage; myxomatous and sarcomatous tissues; islands of squamous epithelial cells	?	?	?
9. Ritter, O.: Ztschr. f. Geburtsh. u. Gynäk. **89**: 266, 1925-26.	58	?	Anterior wall of fundus; polypoid tumor, size of hen's egg, attached by a broad base; coarsely nodular; variegated color; invasion of myometrium	Embryonal muscle cells; myxomatous tissue; cystic glandular occlusions; collagen	Vaginal bleeding for several weeks; physical signs (?)	Removal of uterus including cervix	No data
10. Halter, G.: Zentralbl. f. Gynäk. **50**: 2194, 1926.	47	None	Posterior wall of corpus uteri enlarged, corresponding to a 5 mo. pregnancy; extension into cervical canal, portio vaginalis, and myometrium; no data as to color, consistence, etc.	Embryonal muscle cells; glands; myxomatous tissue	Prolonged vaginal bleeding and foul smelling discharge; shortly before admission, frequent vaginal passage of tissue fragments; physical examination revealed enlarged and freely movable uterus palpable at a level of two fingerbreadths below navel; vagina filled in part with necrotic, and in part with polypoid tumor masses	Total extirpation of uterus and adnexa	Alive and well without pelvic recurrences 3 mo. after operation

11. Gamper, A.: Arch. f. Gynäk. **129**: 878, 1926-27.	54	Para viii	Corpus uteri; large polypoid deeply furrowed, waxy white mass broken up by multiple cavities	Embryonal striated muscle cells; cartilage; glands; fibrillary connective tissue; myxomatous tissue; cysts filled with mucin	Yellowish white, blood-tinged vaginal discharge for 6 wk. before admission associated with intermittent slight pain over lower abdomen; upper pole of mass palpable three fingers above symphysis; corpus enlarged to about size of a fist; uterus freely movable	Hysterectomy	Patient still alive 4½ yr. after operation without evidence of metastases or local recurrences
12. Amolsch, A. L.: Am. J. Cancer **37**: 435, 1939.	57	Para x	Upper posterolateral wall of fundus; dilatation of uterine canal by a large soft, partially hemorrhagic polyp, microcystic, and containing an area of translucent cartilage; miliary metastases in peritoneum and omentum observed at laparotomy; no autopsy	Rhabdomyoblasts; glands; cartilage and bone; myxomatous tissue; malignant polymorphous cell sarcoma	Postmenopausal vaginal bleeding of 3 mo. duration; polyp protruding through external cervical os, attached high in the uterine cavity; complaint of vaginal bleeding 2 yr. later	Complete hysterectomy	Death due to shock 1 day after operation

An investigation of the recorded literature on the subject of vaginal, cervical, and corporeal mixed tumors indicates that the corpus uteri is definitely the least common site of their occurrence. These tumors more or less resemble certain other tumors of the type described by Wilms[8] as mixed tumors in the kidney and elsewhere. They are distinct from sarcomas, rhabdomyoma, and teratoma of the uterus. Their rarity, their remarkably varied structure, the clinical picture they present, and above all, the problems of histogenesis to which they give rise, make, together with a complete list of verified published cases, the recording of each new case an obligation.

CASE REPORT

Mrs. M. H., a 67-year-old white, married, female, para iv, was referred to the Nathan Littauer Hospital on April 1, 1938, for removal of a large pelvic tumor.

Present Illness.—The present illness began nine months before admission with dysuria and frequency of urination, progressive in character. Two months after the appearance of these urinary disturbances, the patient noticed enlargement of the lower abdomen. She complained at no time of pelvic pain, vaginal bleeding, discharge, or of any rectal disturbances. The presenting symptoms which forced her to seek medical advice were dysuria and frequency of urination.

Family History.—Essentially negative.

Past History.—The menstrual history was normal. Catamenia began at the age of 15 years. The menstrual periods occurred at regular intervals of twenty-eight days with an average flow of seven days. Menstruation ceased suddenly at the age of 46 years, and there were no disturbing postclimacteric manifestations.

At the age of 42 years a thyroidectomy had been performed. At the age of 55 years the appendix, right tube, and ovary were removed, at which operation a small "uterine fibroid" was noted. Otherwise, the patient always enjoyed good health.

Physical Examination.—The patient was a moderately nourished, elderly, white female, not acutely ill. The lower abdomen appeared moderately and uniformly enlarged. On abdominal palpation a fixed mass, indefinite in outline, occupying the suprapubic area and extending to the left, could be felt. In addition, moderate tenderness in the right lower quadrant of the abdomen was elicited. Pelvic examination revealed a multiparous introitus, a slight mucoid vaginal discharge, and no external evidences of infection. A mass, hard, fixed, smooth, and not tender, the size of a grapefruit, was felt in the region of the uterine body and appeared to extend into the left parametrium. The cervix was visualized and appeared normal. Otherwise, physical examination did not appear to be remarkable.

Laboratory Data.—Urine: specific gravity, 1.022; acid, 1+ albumin, negative sugar; and 2 to 3 W.B.C. per high-power field. Hematologic: Hgb. (Newcomer), 78 per cent; R.B.C., 3,900,000; W.B.C., 10,100. Differential smear: polymorphonuclear leucocytes, 54 per cent; small lymphocytes, 34 per cent; large lymphocytes, 10 per cent; eosinophiles, 1 per cent; and basophiles, 1 per cent; complement fixation and Kahn tests for syphilis, negative; sedimentation rate, 48 mm. in one hour (Wintrobe); blood urea nitrogen, 17 mg. per cent; phenolsulphonepthalein dye test, total dye excretion of 62 per cent in two hours.

Treatment.—On April 4, 1938, laparotomy was performed under gas-oxygen-ether anesthesia. A uterine mass, hard, smooth and fixed, filled the pelvic cavity and was attached to the sigmoid colon anteriorly and to a loop of ileum posteriorly. The right tube and ovary were absent. The left tube and ovary were normal. Examination of the contents of the abdominal cavity showed nothing unusual. A supravaginal hysterectomy and left salpingo-oophorectomy were performed. Convalescence was uneventful, and the patient was discharged on April 16, 1938.

Subsequent Clinical Course.—The patient remained well for six weeks, but thereafter complained of progressive weakness, anorexia, and loss of weight. She suffered from pain in the left chest. Examination revealed dullness and diminished breath sounds at the left base. Stereoscopic films at this time revealed "metastatic malignancy" involving both lung fields.

On June 11, 1938, the patient was readmitted to the hospital complaining of moderate interscapular pain and weakness. She appeared cachectic, but was mentally alert. The temperature ranged between 97.6 and 100° F., the pulse, between 80 to 110, and the respiratory rate, between 20 to 24. There was mottled dullness with diminished breath sounds throughout both lung fields, especially over the left upper anterior chest. No palpable masses were felt on abdominal examination. On June 14 the patient developed a complete paraplegia at the level of the twelfth thoracic vertebra and died four days later.

GROSS AND MICROSCOPIC DESCRIPTION OF SPECIMEN REMOVED AT OPERATION

Gross Appearance of Primary Tumor in Uterus.—The specimen consisted of a uterus and left oviduct and ovary removed at operation. The uterus was amputated above the cervix. It was roughly pyriform in shape and greatly enlarged, measuring 15 by 20 by 10 cm. in its diameters. Externally its surfaces were smooth and free from any gross abnormal changes of note. On sagittal section the entire wall appeared to be stretched by a large polypoid growth attached to both the anterior and posterior walls by a broad base. This contrasted with the botryoid tumors of the vagina which acquire their gross appearance principally because of the dominance of myxomatous tissue and the space for growth afforded by the vagina. Examination revealed that the entire uterine wall, including the endometrium, was replaced by tumor, and that the uterine cavity was much distended and filled with growth. The surface of the tumor was nodular and not lobulated. The consistence of the growth was generally firm. In color, the growth was predominantly pink to pinkish gray, and mottled with many irregular, soft, friable, opaque, yellow to yellowish brown areas up to 1 cm. in their widest diameter and a few small areas of fresh and old hemorrhage. There were frequent irregular, variably sized areas of smooth, translucent, grayish myxomatous tissue, and an occasional small, hard, irregular mass of bone. No grossly visible cysts were seen. There were no teratomatous structures and no tissues suggestive of cartilage.

The oviduct and ovary showed no gross changes worthy of note.

Microscopic Appearance of Primary Tumor in Uterus.—A large number of representative sections from different parts of the tumor and at various levels were prepared. These were fixed in formalin, Bouin's fluid, Heidenhain's "Susa" fluid, and absolute alcohol, and were stained with hematoxylin and erythrosin, van Gieson, Masson's iron hematoxylin, Mallory's acid fuchsin and aniline blue, Best's carmine for glycogen, Maximow's hematoxylin-eosinazure II for blood cells, Weigert-Pal for myelin sheaths, Bielschowsky-Plien for Nissl substance, Mayer's mucicarmine for mucin, and impregnated for axis cylinders according to the silver impregnation method of Bielschowsky-Agduhr.

The primary growth was composed of a wide variety of heterologous elements and structures among which the embryonal myoblast predominated and formed the essential matrix of the tumor. Only bone marrow and nerve tissue were conspicuous by their absence. Fresh and old hemorrhages into the substance of the tumor were frequent, and many small and large areas of partially to completely necrotized embryonal myoblasts were present.

Embryonal Myoblasts.—(Fig. 1.) These cells were irregularly laid down as variably sized solid islands and interlacing strands. Their individual variation in length and width was marked, ranging from 10 μ to 100 μ or more in length. The cells assumed a wide variety of shapes, appearing round, oval, triangular, pyriform, or even bizarre. Their nuclei varied considerably in size, shape, number, and even in

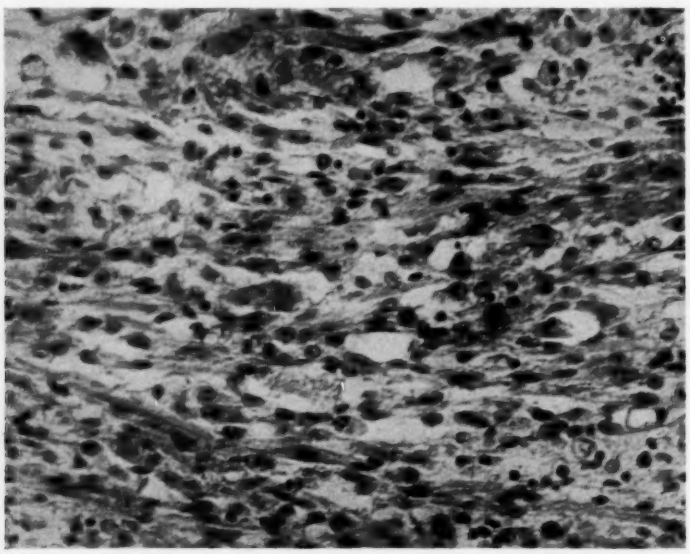

Fig. 1.—Photomicrograph at ×375 from section stained with van Gieson stain showing a field of embryonal myoblasts embedded in a vascularized myxomatous stroma.

chromatin content. However, the majority contained a single, relatively large, central or peripherally located nucleus with a prominent nucleolus, surrounded by a relatively sparse number of fine chromatin granules bounded by a densely staining nuclear membrane. The resemblance of the nucleus to that of a normal ganglion cell in the central nervous system was often striking. Many of the embryonal myoblasts were multinucleated, the nuclei often overlapping each other. Mitotic figures in different stages of development were relatively sparse in number.

The cytoplasm of the myoblasts was abundant and streamed out from the nuclear poles for a variable distance. These cytoplasmic processes did not fuse with each other to form a network.

Practically all of the cells revealed well-developed, delicate, longitudinal striations, consisting of fine bright red, fuchsinophile granules

strung closely together. As a rule, the cross striations were wholly absent or only partly to completely developed in the individual fibers. In the embryonal myoblasts sectioned transversely, the cross-striations were disposed concentrically in the perinuclear cytoplasm. They could be brought into sharp relief by peripheral degeneration in the latter. A definite sarcolemma was not observed. In a few cells paired centrioles were noted in the cytoplasm in close proximity to the nucleus.

The embryonal myoblasts commonly displayed a variable degree of degeneration (Fig. 2). Many of them were reduced to coarsely honeycombed and vacuolated cells with partial to complete loss of their longitudinal and cross-striations. The less severely damaged cells revealed swelling and separation of the longitudinal striations accompanied by karyorrhexis of the nuclei.

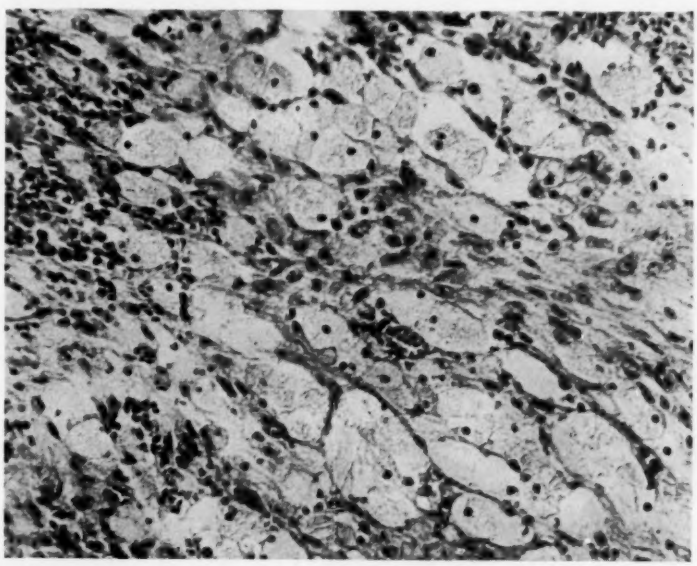

Fig. 2.—Photomicrograph at ×300, showing degenerated and necrotic embryonal myoblasts (hematoxylin and erythrosin stain).

In the sections stained for glycogen, the embryonal myoblasts commonly contained an abundance of glycogen granules indicative of their immature character.

No morphologic transition from embryonal myoblasts to normal adult smooth muscle cells could be traced.

Smooth Muscle.—Van Gieson preparations often reveal isolated strands and bundles of adult, normal appearing, fully differentiated smooth muscle cells.

Glands.—(Fig. 3.) Benign appearing glandular structures, strongly resembling normal endometrial glands of the uterine mucosa, were frequently incorporated within the substance of the tumor. Irregular in outline and dimensions and not surrounded by uterine stroma cells, they were lined by a single flat layer of medium to low columnar

epithelial cells. They revealed no morphologic evidence of secretory or menstrual activity or of malignant transformation.

Myxomatous Tissue.—(Fig. 4.) A striking feature of the tumor was the large number of irregularly distributed areas of mesenchymal myxomatous tissue. They consisted of triangular or stellate-shaped cell bodies from whose points passed long, delicate protoplasmic strands, forming a mesh network containing a slightly granular mucinous material stained pink in the Mayer mucicarmine preparations.

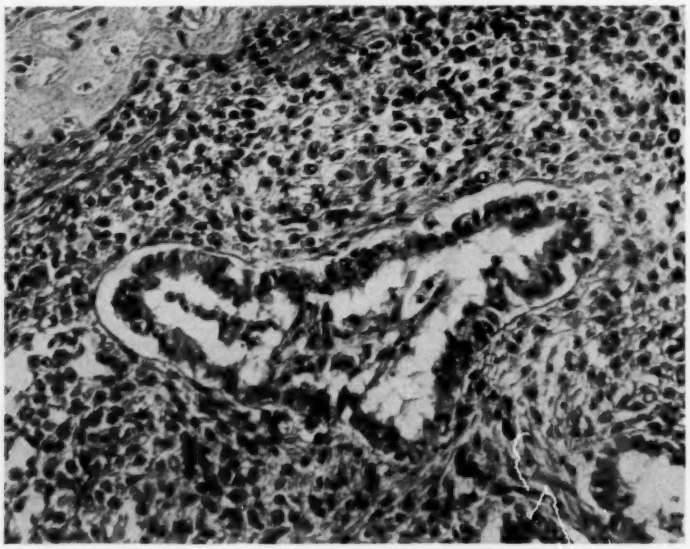

Fig. 3.—Photomicrograph at ×280, showing a gland within the substance of the tumor resembling normal uterine endometrial gland and surrounded by embryonal myloblasts (hematoxylin and erythrosin stain).

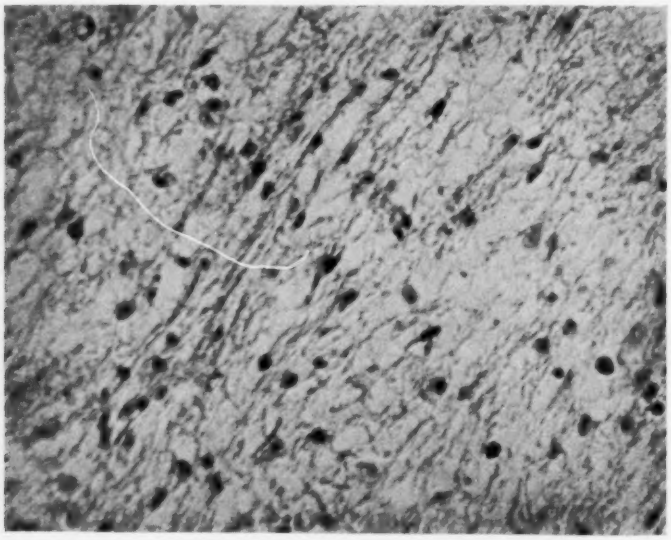

Fig. 4.—Photomicrograph at ×375, showing an island of myxomatous tissue (Mayer's mucicarmine stain).

Adipose Tissue.—(Fig. 5.) There were infrequent irregularly distributed nonencapsulated, small islands of adult nongranular fat cells, varied in size and shape.

Collagen and Reticulum.—There were many small areas and bundles of collagen, sparsely populated by nuclei. The Wilder silver preparations for reticulum showed a large number of wiry and stiff reticulum fibers.

Cartilage.—There were occasional islands of cartilage composed of more or less mature hyaline cartilage cells embedded in a pinkish red

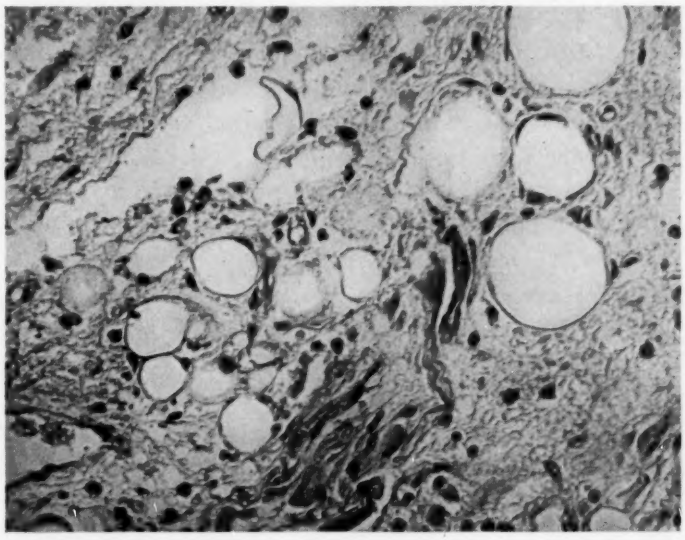

Fig. 5.—Photomicrograph at ×330, showing an area of adipose cells (hematoxylin and erythrosin stain).

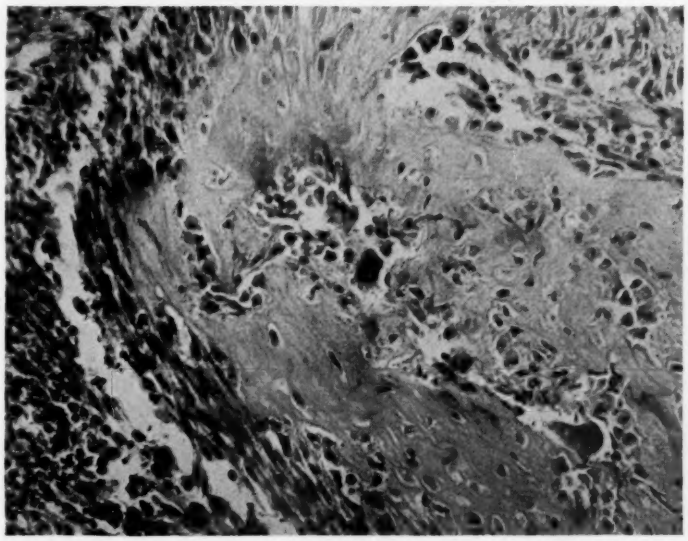

Fig. 6.—Photomicrograph at ×230, showing lamellae of osteoid tissue (hematoxylin and erythrosin stain).

staining matrix and surrounded by a thin zone of spindle-shaped perichondrial cells.

Bone.—Adult osseous and osteoid tissue (Fig. 6) laid down as lamellae and without marrow cells between the latter was observed in only one area.

Lymphatic Tissue.—There were many foci of massed, small round cells unaccompanied by germinal or plasma cells. In the Maximow-stained preparations, the cells corresponded morphologically and tinctorially to normal adult lymphocytes. They were interpreted as such rather than as primitive mesenchymal cells.

Nerve Tissue.—A large number of sections stained for myelin sheaths and Nissl substance and impregnated with silver nitrate for axones failed to reveal any nerve tissue of any description.

Blood Vessels.—The tumor was, in general, richly vascularized by many new formed capillaries and veins. Clumps of characteristic embryonal myoblasts were not infrequently present in the lumina of the larger, thin-walled blood spaces. No other heterologous element was seen within them.

Malignant Degeneration.—There was no evidence of carcinomatous or sarcomatous degeneration.

AUTOPSY

Autopsy revealed a small, much emaciated, white female about 60 years of age. The peritoneal cavity contained a large metastasis over the left anterolateral portion of its wall. Smaller metastases were present over the anterior wall of the pelvic cavity and over the serosal coat of the large intestine. Each pleural cavity contained about 50 c.c. of a blood-tinged fluid, and its visceral and parietal surfaces were studded with many metastases, firm in consistence and predominantly opaque grayish white in color. The lungs and liver contained many scattered, round, metastatic nodules, measuring up to 6 cm. in diameter, and presenting a mottled yellowish red to opaque grayish white color. The lumbar lymph nodes were the seat of extensive neoplastic invasion.

No permission for examination of the spinal cord and vertebral column was granted.

Microscopically the metastases were composed only of embryonal myoblasts in a primitive stage of development. These were often present in the smaller veins of the lungs and liver.

REVIEW OF LITERATURE

Terminology.—The complex structure and composition of the heterotopic mesodermal tissue tumors of the uterus and vagina have given rise to an extremely complex nomenclature. McFarland[9] tabulated a list of no less than 116 terms employed to designate neoplasms which, on the basis of histogenesis and structure, may reasonably be grouped in one class. Often the presence of a dominant tissue element or of a

distinctive type of tissue has led to the confusing use of such terms as chondroma, myxoma, rhabdomyoma, etc. However, Lahm[10] groups the latter as simple tumors unless they are heterologous in nature or the one-sided development of a mesodermal mixed tumor.

McFarland has advocated the use of the term "dysontogenetic tumor" to designate this entire class of neoplasma developing in the urogenital system. This term is too broad in its scope and does not delimit the nature and behavior of the growth.

The term mesodermal mixed or combination tumor first proposed by Kehrer[11] and Meyer[12] is preferable to all others in that it is simple and indicates not only the complex morphologic structure of the growth, but also its relationship to displaced mesodermal embryonal rests. The use of the adjective mesodermal, as Meikle[13] points out, is desirable since it eliminates from this category teratomas containing derivatives of all three germinal layers.

The objection to the term fibro-myxo-chondro-sarcoma lies in its descriptive inadequacy. It suggests that only these elements are present, when, in point of fact, any single one may be absent in a given specimen. Furthermore, it fails to emphasize the presence of embryonal striated muscle cells essential for a pathologic diagnosis, as well as other structural elements.

The term rhabdomyosarcoma employed by Glynn and Blair Bell is satisfactory in one respect in that it indicates the presence of a very characteristic type of cell, the longitudinally and transversely fibrillated embryonal muscle cells. It also connotes the presence of sarcomatous tissue, which may be absent. However, as a descriptive name, it is too limited by virtue of its failure to indicate adequately the composite nature of the tumor. For these reasons it has been rejected.

Pfannenstiel[14] employed the term *traubige Sarkom*, or botryoid sarcoma as it is known in this country and Great Britain, to describe graphically its grapelike character. This term is also unacceptable because a botryoid appearance is by no means always present in the mesodermal mixed tumors arising in the corpus of the uterus. On the contrary, the corpus tumor is almost invariably polypoid in character.

To conclude, it was decided after careful consideration of all the terms proposed to accept that of Kehrer as the most satisfactory in the present state of our knowledge; viz., mesodermal mixed tumor.

Etiology.—There is no clear proof that either age or parity is a factor of etiologic importance. Although the great majority of the cases occur in multiparas, there are insufficient data to draw any conclusions as to the etiologic significance of pregnancy. In addition, it is difficult to explain the average peak age incidence after menopause.

HISTOGENESIS

The occurrence, in an organ developed from the Müllerian ducts, of a neoplasm having tissue components of such wide variety has aroused

much interest and speculation in its genesis. At present, there are two prevailing theories; viz., those of Pfannenstiel and Wilms.

Pfannenstiel has advanced the conception that the series of heterologous elements present in the tumor is derived from normal connective tissue of the uterine mucosa by a process of metaplasia initiated by some indeterminate cause. This theory has today but few adherents. Metaplasia can account for the development of smooth muscle, cartilage, and bone from mesenchymal tissue but not for striated muscle cells. A transition from normal, adult fibroblasts to striated muscle cells does not take place normally. Moreover, the transformation of smooth into striated muscle cells has never been proved. The presence of striated muscle cells is best attributed to an origin from a muscle anlage.

Nicholson[15] states that his case of multiple primary mesodermal mixed tumors can be best explained on the assumption of dedifferentiation and rejuvenation of the stroma of the uterine mucosa. Its cause is not known. It hardly seems reasonable that a physiologically and morphologically ripened tissue such as the stroma of the uterine mucosa can dedifferentiate into such diverse tissues as cartilage, muscle, etc.

Islands of fully differentiated striated muscle cells have been described by Gerode[16] and Nehrkorn[17] in the wall of two uteri removed after puerperal sepsis. These were not associated with a tumor. Mesodermal mixed tumors cannot be ascribed to their presence, although the striated muscle cells alone may well originate from them.

Wilms[18] has proposed a theory of origin based essentially upon Cohnheim's hypothesis of cell rests. He holds that the tumors spring from rudiments of primitive mesodermal tissue displaced and carried down from the lumbar region by the Wolffian body in its descent early in fetal life. This theory is supported by the complicated embryologic development of the genital tract favoring the deposit of cell rests and by the complex structure of the tumor. Careful analysis of all the evidence leads to the conclusion that cell rests originating from the Wolffian bodies are not the source of these tumors. Absence of striated muscle or of its anlage in the Wolffian system, as well as failure of these tumors to develop along the course of the Wolffian duct, controverts the Wilms' theory.

We agree with Mönckeberg,[19] Kehrer, and Lahm that it is more probable that the cell rests arise from the Müllerian ducts after their fusion to form the uterus and vagina. Meyer[20] states that indifferent embryonal cell-rest displacements of the Müllerian ducts are probably very frequent in the region of the uterus and vagina and not rare even in the late months of fetal development. The rests are present chiefly in the deeper layers of the myometrium, especially in the anterior and posterior walls, early in fetal life. A valid objection to this theory is the absence of any proved cases of mixed tumors in the broad ligaments despite the migration of the Müllerian ducts through them. Another objection

which may be leveled not only at a Müllerian but also Wolffian duct origin is the dormancy of the cell rests for several decades. It is impossible, at present, to explain why these rests should slumber for years and then suddenly spring to life despite their association with many pregnancies and monthly ovarian cycles. Meikle has suggested that the cell rests are activated by hormonal disturbances but has offered no evidence as to their nature and behavior, and in point of fact, no proof of their actual existence. There is no demonstration that chronic irritation, constitutional predisposition, infection, etc., are growth stimuli. On the other hand, the strength of the Müllerian duct theory lies not only in the location of the tumor, but also in the pluripotential capacity for differentiation of the indifferent embryonal cells into myxomatous tissue, bone, etc. Additional support for this theory is offered by the rare presence of these tumors in the base of the urinary bladder. It is conceded that this theory is not wholly satisfactory, but it is the best offered so far.

There is much speculation as to which tissues or cells constitute the primitive matrix from which the other heterologous structures are derived. Wilms, Nicholson, and others believe that the embryonal myxomatous tissue is the matrix on the basis of morphologic evidence of a transition between this and other tissues. On the other hand, other students hold that groups of small round cells morphologically resembling lymphocytes represent the common mother tissue. The balance of evidence appears to favor an origin from embryonal myxomatous tissue.

COMPARISON OF MESODERMAL MIXED TUMOR OF CERVIX AND BODY OF UTERUS

Mixed tumors of the cervix are more frequently encountered than those of the corpus, the ratio being about 3:1. There is a striking difference in their age incidence. Tumors of the body occur most often about and after the climacteric, while those of the cervix almost always occur in women during the active sexual decades. Tumors of the vagina predominate in childhood and adolescence.

Both are clinically characterized by vaginal bleeding, foul leucorrhea, fulminating course, and a marked capacity for local recurrences. In microscopic structure they resemble each other closely, but differ from each other in gross appearance. The cervical tumor is almost invariably arborescent in character while that of the corpus is nearly always polypoid in type and possesses a distinct pedicle.

The diagnosis of cervical tumors can be made much earlier and with greater accuracy because of their earlier tendency to produce vaginal bleeding and their accessibility to inspection and biopsy. For these reasons they are not as apt to be confused with benign lesions as may often be the case with corporeal tumors.

GENERAL PATHOLOGIC DESCRIPTION OF MIXED TUMORS OF CORPUS OF UTERUS

Macroscopic Appearance.—Assuming that these tumors arise from cell rests of müllerian duct origin, the corporeal tumors, as would be expected, originate in the wall of the uterus, especially from the posterior wall of the corpus. They lead to a variable and generally globular enlargement of the uterus. The external surface of the uterus is usually smooth except, perhaps, for an occasional fibrous tag or subserous tumor nodule.

The volume of the tumor may attain considerable dimensions, reaching the size of an adult's head, and extending upward out of the pelvic cavity into the abdominal cavity to the level of the umbilicus or above. The tumor constantly bulges out into the uterine cavity, distending it for a variable degree.

In contrast to the well-known arborescent, grapelike form of the cervical type, corporeal tumors appear almost always as polypoid masses, projecting into the uterine cavity from a broad submucosal base. The tumor seldom presents itself as a solitary large polyp attached to the uterine wall by a pedicle.

The growth is usually submucous in location and is either sharply delimited or insensibly fused with the myometrium, which is replaced either in part or in whole by tumor tissue. The mucosa above its attachment is either variably thickened or completely destroyed by tumor as was the case with the tumor herein described. Commonly, the surface of the growth is covered with a variable number of polypoid excrescences.

As would be expected from their genesis, mixed tumors of the corpus reveal a marked variation in their macroscopic appearance, depending upon the number and relative proportions of their structural components. The cut surfaces are lobulated and a variegated and mottled red to brown to pink to grayish white in color, and appear translucent, gelatinous, opaque, and opalescent. Should the embryonal muscle tissue predominate, the color will be essentially grayish pink in color. Cartilage is only occasionally present in sufficiently large amounts to be identifiable as such. The consistence of the tumor is very variable, being very soft and friable in areas of necrosis, and dense and tough in others. Cystic cavities of variable dimensions, lined by rough, necrotic walls and filled with a bloody or foul-smelling purulent fluid, are often present. They may be palpated as areas of distinct fluctuation. Areas of old and fresh hemorrhage are frequent. On section, much tissue juice may ooze.

Carcinomatous degeneration is extremely rare. A certain percentage has been described as containing sarcomatous tissue arising in the tumor growth proper, but this may be confused with primitive spindle-shaped embryonic myoblasts. In the absence of sections stained with van

Gieson, the exact frequency of sarcomatous degeneration cannot be determined with accuracy.

Microscopic Appearance.—The microscopic structure of the tumor is relatively more characteristic and important than the gross changes. Only by careful microscopic examination of a large number of representative and suitably stained blocks of tissue is it possible to establish the true nature of the tumor. Although its structure is theoretically broad, and, therefore, extremely complex, all of the possible heterologous elements and tissue may not be present. Furthermore, extensive necrosis and hemorrhage often lead to their destruction and disappearance. Therefore, any single structure may be absent, but the presence of embryonal muscle cells is essential for pathologic diagnosis.

Embryonal Myoblasts.—These are present in various stages of development and in a variable number. Thus, in the cases of Gamper, Lawen, and our own, the bulk of the tumor consisted of embryonal striated muscle cells. The more primitive cells are spindle-shaped with a relatively large oval or ovoid single nucleus, vesicular in character, and frequently presenting mitotic figures. They do not constitute the stroma of the tumor but are an integral part of it. Unless stained with van Gieson's method, they may be rapidly confused with sarcomatous cells.

The larger and more fully developed cells are spindle-shaped or round, depending upon the plane of the section, and either long or short. They are arranged in groups or bundles. Their cytoplasm, which tapers to a blunt end, constantly presents a well-defined longitudinal fibrillation. A smaller number appear transversely fibrillated in part or in whole. With suitable stains the cytoplasm may show glycogen granules, a sign of their cellular immaturity as first pointed out by Marchand. The presence of fibrillation alone or associated with glycogen is an important cellular diagnostic criterion. The cells are either uni- or multinucleated. The nuclei are large, occupying the greater part of the cell, and characteristically vary in position. They appear irregular in outline and either vesicular or hyperchromatic. They show single or multiple mitotic figures. In view of their invasive properties, their presence in large numbers, especially within blood vessels, is a sign of grave omen.

Smooth Muscle.—Isolated strands or bundles of adult smooth muscle cells, staining a characteristic brownish yellow color with van Gieson's stain, are frequent.

Myxomatous Tissue.—This varies in amount and is morphologically characteristic. The cell bodies are stellate or triangular, with long protoplasmic strands streaming from their points to form a loose network containing a clear or slightly granular material. The nuclei of the cells are single and either round or oval.

The test for mucin is positive only in the older and more differentiated areas, as Nicholson demonstrated in his tumor, and as we were able to confirm in our own case. This would indicate that the tissue is not an edematous connective tissue as stated by Pfannenstiehl. Likewise, there is no evidence to indicate that the tissue constitutes a true myxoma.

Cartilage.—A frequent and characteristic element is hyaline cartilage. It is generally immature and exists as small islands surrounded by a perichondrium composed of spindle cells.

Bone, Osteoid Tissue, and Bone Marrow.—Osteoid tissue or bone is distinctly uncommon. True bone marrow has not been described.

Nerve Tissue.—This has not been found in the verified cases.

Adipose Tissue.—Fat is uncommon and is usually present in minute areas. It consists of adult, nongranular cells morphologically resembling in their distribution and in their variation in size and shape those encountered in simple, benign lipoma.

Glands.—Glands closely resembling those normally present in the endometrium are often incorporated within the substance of the tumor. The few observations made of them do not indicate any of the changes characteristic of the proliferative and secretory phases of the menstrual cycle. Despite their resemblance to normal endometrial glands, there is no doubt that they are not persisting glands. It seems inconceivable that these glands, completely surrounded as they are by a wide variety of heterologous elements, should have survived destruction by the invading tumor. Therefore, we agree with Läwen that they are probably derived from embryonic cell rests and actively participate in the construction of the tumor.

Lymphocytes.—Multiple foci of small round cells, morphologically and tinctorally resembling lymphocytes, are often present.

Squamous-Cell Epithelium.—Occasionally, small islands of simple squamous epithelium may be seen.

Columnar Epithelium.—A columnar epithelial lining completely covering the tumor has been described, but this was not present in our own case despite the examination of a large number of tissue blocks taken from the surface of the tumor.

Blood Vessels.—Usually these tumors are richly vascularized by thin-walled blood vessels lined by a single layer of endothelial cells.

Metastases and Local Recurrences.—There is a definite tendency to simplification of the complex structure of the parent uterine tumor in the metastases and local recurrences so that the microscopic picture in the latter is more simple and uniform and dominated, as a rule, by embryonal myoblasts.

Local Extension and Metastases.—Although approaching chorionepithelioma in its malignant behavior, it is not yet possible to indicate with accuracy the precise local and distant extensions of this tumor because of the lack of data. Only a few complete autopsies have been per-

formed, and the operative findings recorded in the literature are, as a rule, incomplete.

As with other malignant tumors, the mode of spread is largely governed by the aggressive nature of the tumor cells and by the texture and vascular and lymphatic richness of the stroma of the growth. Local extension into the uterus takes place essentially by infiltration of preexisting or potential tissue spaces. The distant metastases are readily accounted for by venous invasion favored by the infiltrative destruction of the capillaries and veins, especially by the myoblasts. The lymphatics apparently play but a minor role as a channel of extension for local or distant metastases. There is no direct relationship between the extent and degree of the myometrial invasion and the number and distribution of the distant metastasis.

Despite the marked tendency to local invasion and postoperative local recurrences, the parametrium, bladder, and rectum are not invaded. Extension into the cervix with effacement of the cervical canal and deviation of the normal cervical axis has been observed only in the cases of Halter and Herb (Table I). Except for ovarian metastases in Nicholson's case, there is no other instance of invasion of the tubes or ovaries.

Although the lymphatics of the corpus uteri drain into the lumbar lymph nodes, metastases to them occurred only in our own case.

The pleurae, lungs, liver, and pelvic and abdominal peritoneum are the most common sites of remote metastases. In our own case, the pulmonary metastases were composed wholly of embryonal myoblasts.

PATHOLOGIC DIAGNOSIS AND PATHOLOGIC DIFFERENTIAL DIAGNOSIS OF MESODERMAL MIXED TUMORS OF CORPUS UTERI

The microscopic diagnosis of these tumors should offer no difficulty provided that a large number of representative blocks of tissue differentially stained with van Gieson or with one of Masson's trichrome stains are carefully examined. The diagnosis can be established with certainty only by the demonstration of embryonal myoblasts in combination with one or more other heterologous elements such as myxomatous tissue, cartilage, glands, etc. The reason for the necessary presence of the embryonal myoblasts is that its presence can be accounted for only on the basis of an origin from displaced embryonal cells. Although essential for diagnosis, the mere presence of striated embryonal muscle cells alone does not warrant the diagnosis of mesodermal mixed tumor unless it can be shown that rhabdomyoma or rhabdomyosarcoma is a one-sided development of a mixed tumor. Their presence in association with heterologous elements serves not only to settle the diagnosis but also to eliminate such possible sources of confusion as corporeal carcinoma, endometrial polyp, fibroma undergoing ossification or cartilaginous changes, fibromyoma with or without calcification or occasional ossification, inflammation with diverse secondary metaplastic processes, chondromas, lipomas, etc.

The striated embryonal muscle cells in the absence of differential staining can be readily overlooked or confused with sarcomatous cells. An early tendency to degeneration and necrosis may obscure the microscopic picture and increases the chances of failure not only in detecting embryonal myloblasts but also other heterologous elements. Diagnostic curettage not only may fail to reveal the true nature of the tumor, but also may be actually misleading if the curette fails to scrape away a characteristic portion of the tumor.

A corporeal sarcoma, arising either in the mucosa or myometrium, especially if polypoid, grossly resembles a certain type of mesodermal mixed tumor of the corpus. The characteristic "raw pork" appearance in sarcoma described by Cullen should suggest the true nature of the tumor. However, despite the wide limits of variation of the cell structures of sarcoma, the combination of embryonal myoblasts and other constituent elements readily differentiates the two conditions. The occurrence of a sarcoma in a preexisting fibromyoma is diagnostically decisive in that there is no proved instance of such a development in mesodermal mixed tumor.

Mixed tumor is distinguished without difficulty from true teratoma of the uterus by the absence of rudimentary organlike masses of fetal tissues derived from all three germinal layers and present in a disorderly fashion.

Rhabdomyoma is rarely encountered as a tumor but occurs most commonly in or adjacent to the genitourinary system. Instances of this tumor have been described as arising in the uterus, vagina, and ovary. Both tumors contain embryonal myoblasts in various stages of differentiation, but the complex nature of mesodermal mixed tumors readily differentiates it from rhabdomyoma.

Abrikossoff's "*Myoblastenmyome*"[26] is another tumor which may be confused with mesodermal mixed tumor in that it arises from primitive embryonal myoblasts. The growth occurs most commonly in tissues and organs normally containing striated muscle cells, such as the tongue and voluntary musculature. However, it may arise in situations where striped muscle is not normally present. Therefore, its occurrence in the uterus is possible, although a careful search of the literature has failed to reveal any primary instances of this tumor in the uterus. Grossly, this tumor differs sharply from mesodermal mixed tumor, appearing as a small pale red or yellowish growth with or without areas of hemorrhage. The absence of longitudinal or transverse striations and of glycogen in the large and characteristically granular undifferentiated tumor cells of *myoblastenmyome* as well as of heterologous elements are decisive in differentiation.

SYMPTOMS

The symptomatology is essentially similar to that of corporeal carcinoma of the uterus. Postmenopausal bleeding and foul discharge

are the chief presenting symptoms. The hemorrhage may be profuse or slight. Frank bleeding is readily explained by the tendency to extensive necrosis and ulceration in a large tumor in which the vascular supply fails to keep pace with the rapidity of growth.

Pelvic distress and lower abdominal pain may occur but are usually late in appearance. They are varied in character, being either slight or severe, intermittent or continuous.

In contrast to cervical cancer, symptoms referable to hydronephrosis and pyonephrosis do not occur. Compression of the ureters by the tumor or actual invasion of the bladder did not occur in our case and has not been described. This may be due to the fulminating malignant character of the tumor, so that insufficient time elapsed for the development of these complications. In point of fact, urinary symptoms, such as dysuria and increased frequency, are not the rule. A review of the literature failed to reveal any symptoms attributable to pressure upon the rectum.

There are a marked anemia, cachexia, and debility in the terminal stages of the disease.

PHYSICAL SIGNS

The growth is centrally located in the uterus, usually regular and rounded in contour, and in consistence is comparable, as a rule, to that of a fibromyoma. If large, it is readily felt on abdominal palpation and may even be palpated at or above the level of the umbilicus. Most frequently the mass is freely movable because of its tendency not to invade the parametria. Since there is rarely invasion of the adnexa, no masses are felt in the fornices. The growth may project through the cervical canal and even into the vagina as a friable, broken-down mass. In von Franqué's[22] case a tumor the size of a man's head was felt through the dilated cervix as a soft, polypoid mass, in part degenerated, and discharging a yellowish, purulent secretion. Again in Halter's case the vagina was filled in part with a necrotic mass and in part with polypoid tumor masses.

On examination the findings most characteristic of a mixed tumor of the corpus uteri are its large, smooth, rounded contour, and absence of fixation.

CLINICAL DIAGNOSIS

The accurate clinical diagnosis of the disease is impossible because of the origin of the growth in the myometrium, so that curettage in the early stage is not likely to reveal changes indicative of the lesion. The tumor must be distinguished primarily from the more common postmenopausal causes of vaginal bleeding and discharge, such as carcinoma of the corpus and cervix uteri, sarcoma, myoma with secondary sarcomatous development, and granulosa-cell carcinoma. The most confusing condition in the clinical differential diagnosis is corporeal car-

cinoma of the uterus. At best mesodermal mixed tumor can be suspected on the basis of a rapidly growing, freely bleeding, smooth, large, definitely demarcated, postmenopausal fundal tumor. Both develop typically after menopause and their clinical pictures resemble each other except for the differences in the rapidity of their course. The final differentiation of the two conditions rests upon a careful examination of a large number of representative and suitably stained sections.

It is highly doubtful whether visual observation of the tumor projecting into the vagina would lead to correct diagnosis.

COURSE AND PROGNOSIS

The prognosis is uniformly unfavorable, rivaling that of chorionepithelioma. Apart from a certain percentage of deaths occurring after operation, all of the verified cases succumbed within six to twelve months or less after the onset of the initial symptoms regardless of the type of treatment instituted. The only single exception was the patient of Gamper,[23] who survived four and one-half years at date of publication in 1926. There are no five-year cures.

Although the evidence is still inadequate, it would appear from our own case and from those of Läwen and a few others that a preponderance of embryonal myoblasts in the primary growth is an unfavorable sign in view of the propensity of these cells to produce metastases.

Most of the patients have died in a state of malignant anemia and cachexia due to local pelvic recurrences and remote metastases to the liver and lungs.

TREATMENT

If it has been shown with reasonable certainty that remote metastases have not developed, removal of both tubes and ovaries and the entire uterus is indicated. This is warranted by the gravity of the disease, the early invasion of the blood stream, and the speed with which it leads to a fatal termination.

Radical pelvic surgery should be followed by a course of deep x-ray therapy. The law of Bergonie and Tribondeau[24] states that the radiosensitivity of a tissue is proportional to its reproductive capacity and inversely proportional to its degree of differentiation. Scott[25] has furnished ample evidence to show that radioresistance increases with the change from the embryonal to the adult state. The most spectacularly sensitive growths are Wilms' tumor of the kidneys, seminoma of the testicle, lymphoepithelioma of Schmincke, embryonal carcinoma of the ovary, and lymphosarcoma. Inasmuch as the myoblasts usually form the bulk of the tumor and are embryonic, undifferentiated cells, postoperative deep x-ray therapy is worthy of a trial. There are no cases on record cured for a five-year period by radium or deep x-ray therapy alone.

SUMMARY

Cases of mesodermal mixed tumors of the body of the uterus were collected from the literature and were critically analyzed. An additional case of our own has been described. In the light of present evidence, an origin from embryonal cell rests of the müllerian duct appears to be the most acceptable today but is not completely satisfactory.

This group of tumors has been demarcated from other complex tumors of the uterus, such as teratoma, rhabdomyoblastoma, complex sarcomas, etc., by the adoption of certain pathologic criteria. The necessity of the presence of embryonal myoblasts in association with one or more heterologous elements for pathologic diagnosis was emphasized. Attention has been drawn to the grave prognostic significance of a predominance of embryonal myoblasts in the primary growth due to their propensity in invading the blood stream.

The clinical picture of these tumors is described. Due to early extension into the blood stream, complete removal of the uterus and its appendages is indicated. Postoperative deep x-ray therapy is worthy of a trial because of the essentially embryonal character of the tumor. No five-year cures have been reported in the literature.

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NONTRAUMATIC INTRACEREBRAL HEMORRHAGE WITH CLOT FORMATION

A Report of Six Operative Cases

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THE incidence of subcortical hemorrhage with clot formation without history of trauma seems relatively low. Either this is due to lack of recognition of the syndrome or to the actual infrequency of the condition. The etiology of this syndrome continues to be a subject of much controversy. Because of these factors, I feel that it is pertinent to report six cases of nontraumatic subcortical hemorrhage with clot formation and to review the literature.

ETIOLOGY

Charcot and Bouchard[1] introduced the theory, and adduced evidence from cases, that such hemorrhage was the direct result of the rupture of miliary aneurysms. This theory prevailed in textbooks and writings on the subject for many years. Globus and Strauss,[2] in 1927, reviewed the literature and came to somewhat different conclusions. They stated, from their own experience, the belief that spontaneous intracerebral bleeding was the consequence of (1) an area of softening about an arteriosclerotic vessel and (2) hemorrhage from the previously weakened vessel. They believed, along with many of the older pathologists, that the hemorrhage is the result of rupture of a diseased blood vessel which may or may not have aneurysmal dilatation. These two theories have numerous adherents. Neither theory, however, will explain the occurrence of spontaneous intracerebral bleeding in every patient, both young and old. Intracerebral bleeding with clot formation has been a common autopsy finding and subsequent search has often failed to reveal the expected aneurysmal dilation of an intracerebral vessel. Moreover, softening of brain tissue about blood vessels can hardly be given as a cause of intracerebral bleeding in a young individual without primary general or localized arteriosclerosis.

CASES FROM LITERATURE

Few neurosurgeons have had the temerity to consider operation advisable in patients with evidence of spontaneous intracerebral hemorrhage. Some of these patients are often very poor operative risks and operation would indeed be but a feeble gesture. There are some instances, however, where operative procedures are definitely indicated. There have been sporadic reports from the literature from time

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to time of operative intervention with some degree of success in localized intracerebral bleeding. I have collected seventeen cases in which there has been operative intervention, cases of spontaneous bleeding into cerebral tumors, rupture of lenticulostriate artery, middle meningeal hemorrhage; instances of post-traumatic bleeding are not included (Table I).

TABLE I

DATE	SEX	PRE-OPERATIVE DIAGNOSIS	SURGEON	AGE	DURATION OF SYMPTOMS	OPERATIVE RESULT
1903	M		Cushing[8]	40	36 hr.	Death, pneumonia 2 days
1906		Hemorrhage	Spiller[7]	40	6 wk.	Death
1933	M	Tumor	Adson and Craig[4]	37	6 wk.	Recovery
1929	F	Tumor	Adson and Craig	20	6 wk.	Recovery; death 3 mo., *Streptococcus viridans*
1932	M	Tumor	Adson and Craig	25	13 days	Recovery
1932	F	Tumor	Adson and Craig	30	5 wk.	Recovery
1934	M	Tumor	Adson and Craig	46	10 days	Recovery
1934	M	Tumor	Adson and Craig	35	6 wk.	Death on ninth post-operative day
1932	F	Tumor	Bagley[3]	48	22 mo.	Death, hemorrhage into cavity
1932	F		Bagley	39	5 hr.	Death, 10 days, pneumonia
1932	M		Bagley	49	6 mo.	Death
1932	M		Bagley	43	6 mo.	Recovery
1932	M		Bagley	35	1 hr.	Recovery
1932	F		Andre-Thomas, Schaeffer, de Martel, and Guillaume[10]	37	2 mo.	Recovery
1927	F	Tumor	Krone and Mintz[6]	54		Recovery
1933	M	Hemorrhage	Penfield[9]	14	5 days	Recovery
1933	F	Hemorrhage	Penfield	40	6 days	Recovery; sudden death 6 mo. later

From a study of these cases certain things are apparent. Eight of these 17 cases were operated upon with diagnosis of intracranial neoplasm. Five of the 6 operative cases which I am adding to this number were likewise operated upon with a diagnosis of brain tumor. The ages ranged from 14 to 54 years. Duration of symptoms previous to time of operation ranged from one hour to six months.

Spiller,[7] in 1908, stated that the duration of life of patients with hemorrhage into the brain ranged from five hours to two months. The cases listed above show this to be definitely on the pessimistic side. Of these 17 cases, there were 11 operative recoveries. Cushing's[8] case, in 1903, died of pneumonia on the second day. Penfield's[9] second case, reported in 1933, died suddenly six months postoperatively; post-mortem was refused. One of Adson and Craig's cases, operated upon in 1929, died of *Streptococcus viridans* three months postoperatively; post-mortem was refused. In Bagley's series there were 3 operative deaths, 1 with hemorrhage into the cavity after evacuation of the clot, 1 with pneumonia after ten days; post-mortem was refused on the third case. In Spiller's case, reported in 1906, the patient died shortly after operation. These results would lead one to believe that, in certain carefully selected cases, operation might be the treatment of choice rather than the more or less watchful waiting of other years. The period of time elapsed from onset of symptoms to the operation, in the above cases, where a fatality resulted, ranged from thirty-six hours to six months. In those sustaining operative recovery, the time elapsed varied from one hour to six months. Time elapsed from onset of symptoms would thus not appear to be a good criterion as to whether or not operative intervention would be successful. The age of the patient would likewise appear to have little bearing on the outcome. The average age of the recovered cases and those who died was approximately the same. Furthermore, the percentage of recovery, with ultimate favorable prognosis, would seem actually to make one more enthusiastic than many a similar series of patients operated upon with a diagnosis of brain tumor.

ANALYSIS OF CASES, INCLUDING 6 CASES BEING REPORTED

A study of the symptoms and signs exhibited by these 23 patients is interesting and informative (Table II).

Headache and unilateral motor weakness were the predominating symptoms, being present in 20 and 21 instances, respectively. The blood pressure was elevated in only 6 instances. Convulsions were exhibited by 2 patients. Choked disks were present 14 times. Five patients had a hemianopsia, the lesions in these cases being distributed about evenly between the temporal and occipital areas. Aphasias were present in 4 instances and pyramidal tract signs in 13.

The lesions were distributed as follows: temporal, 14; occipital, 3; frontal, 4; temporal-parietal, 1; cerebellar, 1.

I have operated upon the last 6 cases included above with 5 operative recoveries and with a satisfactory clinical result in each case.

CASE REPORTS

CASE 1.—K. K., aged 17 years, was admitted to St. Luke's Hospital on Oct. 19, 1935, with a chief complaint of headache, blindness, nausea, and vomiting of one week's duration. One week before entering the hospital, he noted a sharp con-

TABLE II

DATE	HEADACHE	WEAKNESS	EYE SIGNS	FOCAL SIGNS	LESION	BLOOD PRESSURE
1903	Absent	Left	Choked disks	Difficult speech	Left temporal	300
1906	Absent	Right	Choked disks; homonymous hemianopsia	Right hemiplegia	Left temporal	
1933	Present	Right	Choked disks	Difficult speech	Left frontal	110
1929	Present	Left	Choked disks		Right temporal	105
1932	Present		Homonymous hemianopsia	Aphasia	Left temporal	110
1932	Present	Right	Ptosis right	Right hemiplegia; right seventh	Left temporal; parietal	100
1934	Present	Left			Right frontal	125
1934	Present	Left	Choked disks		Left frontal	110
1932	Present	Right	Choked disks	Right hemiplegia	Left temporal	200
1932	Present	Right	Choked disks	Right hemiplegia	Left temporal	220
1932	Present	Right		Right hemiplegia	Left temporal	210
1932	Present	Right	Choked disks; homonymous hemianopsia		Left temporal	120
1932	Present	Right	Choked disks	Right hemiplegia	Left temporal	160
1932	Present	Left	Choked disks	Left hemiplegia	Right temporal	
1927	Present			Central right seventh	Cerebellar	120
1933	Present	Right		Hemiplegia right Aphasia	Left temporal	
1933	Present	Right	Choked disks	Aphasia	Left temporal	
1935*(1)	Present	Left	Choked disks	Left Babinski and Oppenheim	Right occipital	116
1935*(2)	Present		Altitudinal hemianopsia		Right occipital	120
1936*(3)	Present	Left		Left Babinski; reflexes increased	Right temporal	118/86
1938*(4)	Present	Left	Homonymous hemianopsia; choked disks	Left Babinski; ankle clonus; absent abdominals	Right occipital	110
1935*(5)	Present	Left arm		KK and AJ Left > right	Right frontal	140
1940*(6)	Present	Right	Early choked disks	Right Babinski; reflexes hypoactive	Left temporal	108/74

*Author's cases.

tinuous pain over his right eye. One hour later he suddenly became blind. Vomiting, projectile in type, began shortly thereafter. He was taken home from school and was seen by his physician. Two days later he was seen in consultation at another hospital in the city; operation was advised and refused, as he seemed to be improving. Two days before entry to St. Luke's Hospital the patient noted some return of light perception but could not see definite objects. Physical examination showed: temperature, 99.2°; pulse, 66; respiration, 24; and blood pressure, 116/58. The remainder of the physical examination was negative. Neurologic examination revealed the left pupil larger than the right, both reacting to light and accommodation. Examination of the fundi revealed bilateral choked disks. There was slight

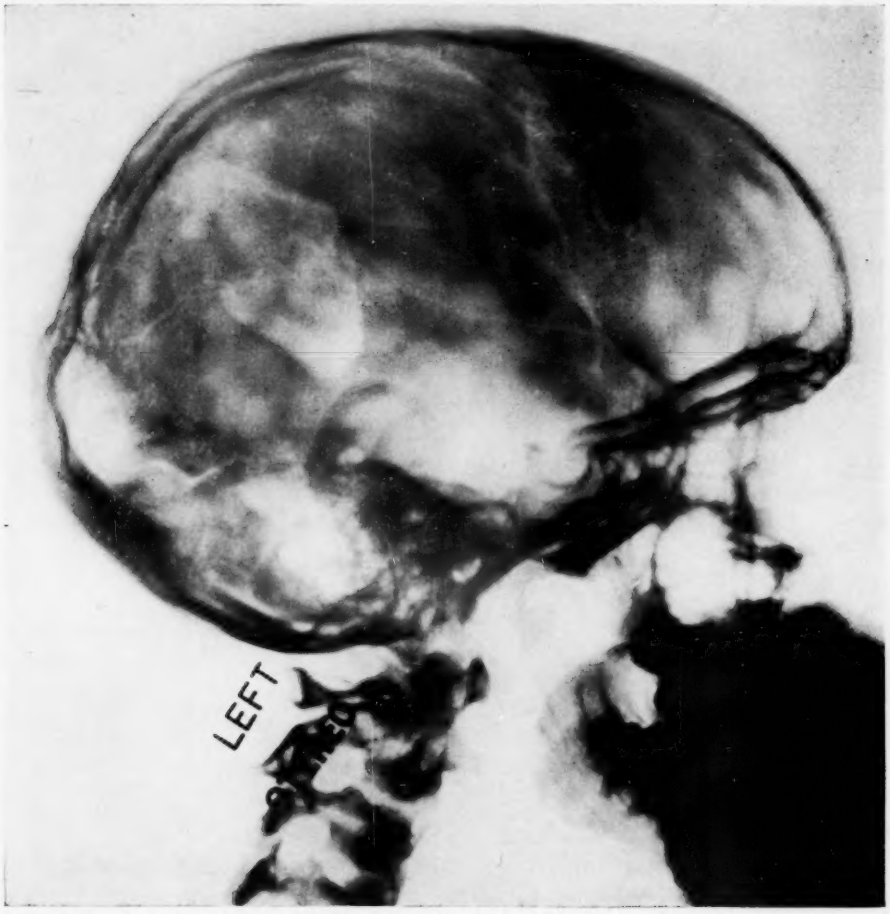

Fig. 1.—Case 1 (K. K.). Air was injected into lesion in right occipital region.

motor weakness of the entire left side without disturbance of sensation. Babinski and Oppenheim were present on the left. The other reflexes were not remarkable. A ventriculogram was done on Oct. 21, 1935, and a lesion demonstrated in the right occipital lobe (Figs. 1 and 2). On the following day a craniotomy was done, a right occipital flap being turned. A small greenish blue area was found on the cortex of the right occipital lobe. A small incision was made through this area with the electrosurgical knife. An organized clot about the size of a lemon was then uncovered and evacuated with suction. Bleeding was controlled and the bone flap replaced. The cavity was filled with Ringer's solution and the wound closed without

drainage. Convalescence was uneventful and he left the hospital seventeen days after entry. There was a residual left homonymous hemianopsia which has gradually, though not entirely, cleared.

CASE 2.—C. B., aged 65 years, was admitted to St. Luke's Hospital on Nov. 24, 1935, with a chief complaint of blindness of three months' duration. On the morning of Aug. 10, 1935, the patient awakened and was unable to see. After about two weeks his vision slowly returned. Two weeks before entry and two and one-half months after the original attack, he had another episode, resulting in total blindness. For the two weeks preceding hospital entry, light perception only was present. There was no paralysis, vertigo, vomiting, or feeling of illness. Physical examination was negative throughout. The blood pressure was 120/90. Neurologic examination

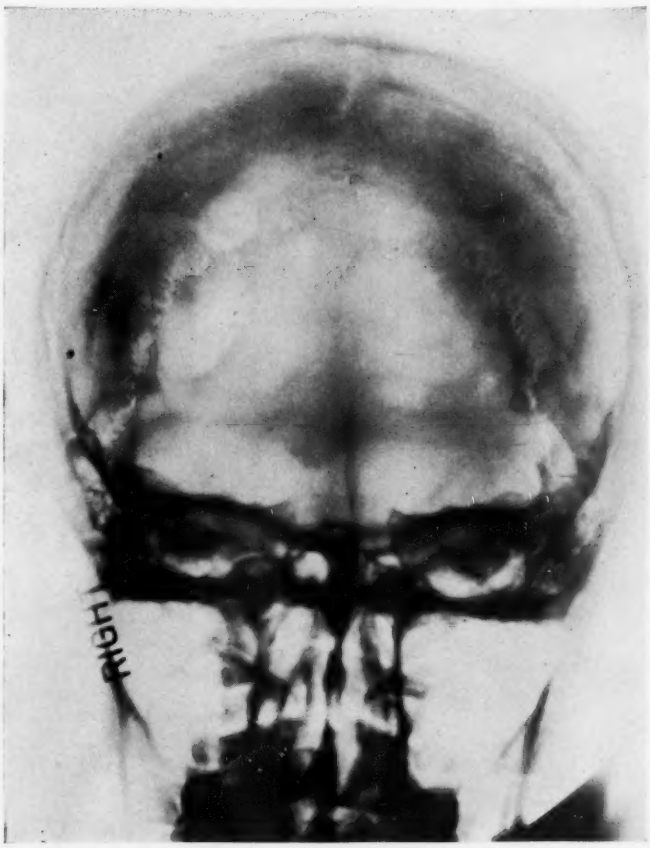

Fig. 2.—Case 1 (K. K.). Anteroposterior view of patient shown in Fig. 1.

revealed an altitudinal hemianopsia without papilledema. There was no sensory or motor weakness. Reflexes were normal throughout, except that there were absent abdominal reflexes on the right. A ventriculogram was done on Nov. 29, 1935 (Figs. 3 and 4), at which time a right occipital lobe lesion was demonstrated. On Dec. 3, 1935, a right occipital flap was turned and a large subcortical clot about the size of a tennis ball along with some brain cortex was removed. The center of the clot contained about 70 c.c. of fluid. The wound was closed without drainage. The patient left the hospital on the eleventh postoperative day. When last contacted on Dec. 15, 1936, this patient was doing very nicely. He had a slight residual left homonymous hemianopsia.

CASE 3.—M. C., aged 32 years, was admitted to St. Luke's Hospital on March 23, 1936, with chief complaint of headache, paralysis of left arm, and paresis of the left leg of two and one-half years' duration. Two and one-half years before entry the patient noticed a sensation of numbness in thigh on the left. A few days later her left leg became paralyzed and she began to have jerking movements of the left leg and arm. Three months before entry these convulsions became more frequent. During this time, she began having headaches of a very severe nature. She noted blurring of vision and vomited on a few occasions. Past history was not remarkable. Physical examination showed: temperature, 98.6°; pulse, 100; respiration, 24; blood pressure, 118/86. Neurologic examination showed cranial nerves intact

Fig. 3.—Case 2 (C. B.). Lateral view, showing lesion in right occipital lobe.

and marked motor weakness of the extremities on the left. There was no spasticity. There was no Babinski reflex, an ankle clonus, and slight increase of reflexes on the left. Visual fields were normal. An encephalogram was done on March 26, 1936, and showed xanthochromic fluid without visualization of the ventricles. On March 30, 1936, an exploratory craniotomy was done. A right temporal parietal flap was turned and, in attempting a ventricular puncture, a large cyst was encountered. The cortex was incised behind the motor area and the region of the arm center and about four ounces of old blood and clots were removed. A small piece of tissue was removed for microscopic examination. The wound was closed in the usual manner

without drainage. The patient had an uneventful postoperative course. Examination of the specimen microscopically revealed arteriosclerosis with hemorrhage and brain softening. The patient was discharged on April 12, 1936. She was walking fairly well with some residual spasticity of left arm and leg. She was last seen by us on July 26, 1936.

CASE 4.—W. S., aged 11 years, was admitted to Deaconess Hospital on Oct. 3, 1938, with the chief complaints of blurring of vision, loss of the lateral field of vision on the left, dizziness, nausea, and vomiting. Two days previous to hospital admission the patient had had a severe headache, followed by marked nausea and vomiting, blurring of vision, and loss of the lateral field of vision, and these persisted until admission to the hospital. There was no history of trauma. Physical examination was negative throughout. The blood pressure was 110/60. Neurologic examination revealed bilateral choked disks, left facial weakness, absent abdominal and cremasteric reflexes on the left, and hyperative reflexes on the whole left side. There was a left Babinski and a suggestive ankle clonus. Examination of the visual fields revealed a left homonymous hemianopsia. A ventriculogram was done on Oct. 4, 1938.

Fig. 4.—Case 2 (C. B.). Posteroanterior view, demonstrating dilated right lateral ventricle.

A lesion was demonstrated in the right occipital lobe and an occipital flap was turned. A large subcortical clot was discovered in the occipital lobe. Because the brain had the appearance of tumor, a large portion of the occipital lobe was resected. A decompression was done and the wound was closed in the usual manner without drainage. The postoperative course was uneventful. Microscopic sections of excised portion of the occipital lobe showed no evidence of tumor. The patient was discharged from hospital Oct. 19, 1938. This patient has returned to his normal activities. He has a slight residual left homonymous hemianopsia.

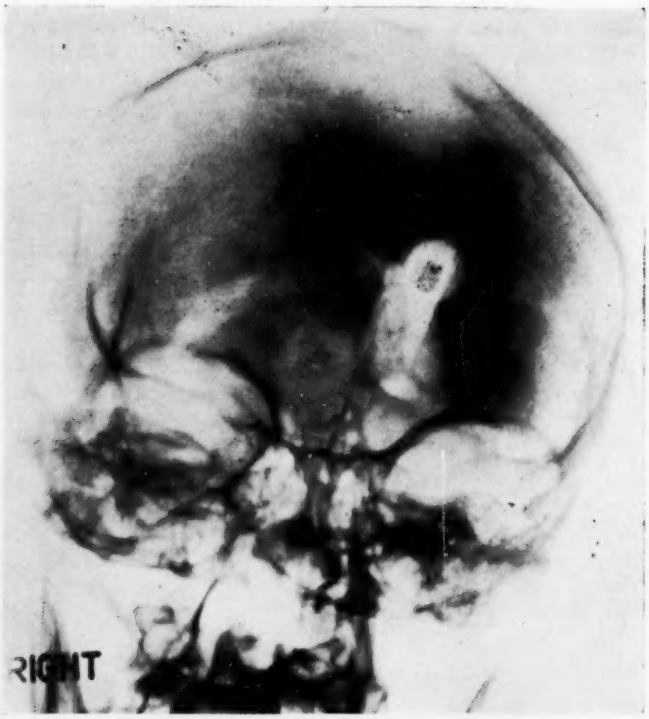

Fig. 5.—Case 5 (J. C.). Posteroanterior view. Ventricular system depressed and shifted to left.

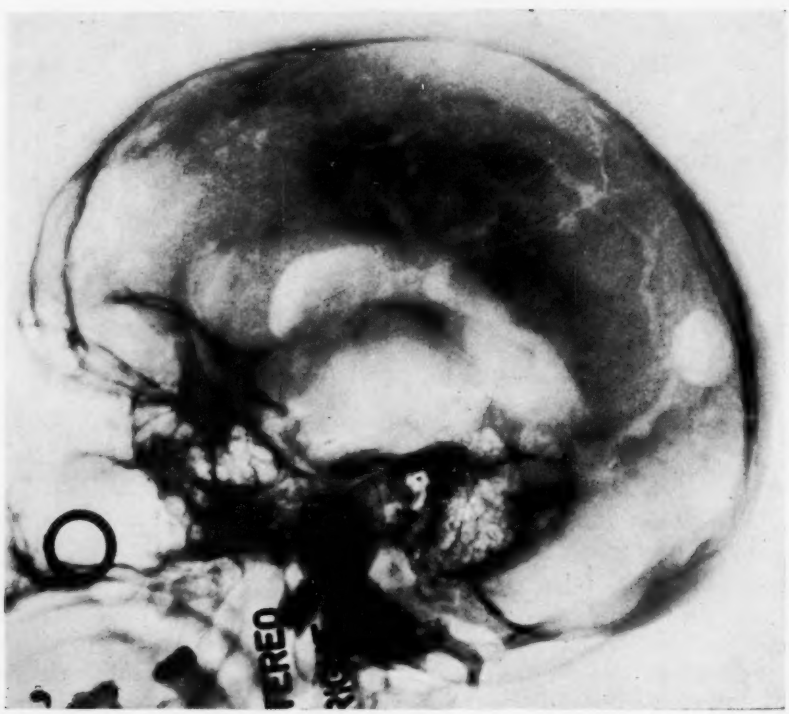

Fig. 6.—Case 5 (J. C.). Lateral view. Right lateral ventricle compressed; anterior portion depressed. Reduction in capacity of whole ventricle.

CASE 5.—J. C., aged 50 years, was admitted to St. Luke's Hospital on March 11, 1940, with a chief complaint of recurrent headaches of several years' duration. About six years before the present hospital entry, she was studied at another hospital because of severe recurrent headaches. She had had migraine attacks since early youth, several of these attacks requiring hospitalization. The present attack began on the evening of Feb. 28, 1940, with very severe headache, nausea, vomiting, cramps in the legs, and pain in the chest. Physical examination, at that time, revealed a somewhat lethargic woman of 50 years of age, apparently quite weak and complaining of right temporal headache. The blood pressure was 140/100. Physical examination was otherwise not remarkable. Neurologic examination showed normal fundi and slight hyperactivity of knee jerks and ankle jerks on the left. There was

Fig. 7.—Case 6 (M. K.). Left lateral view. Filling defect in left lateral ventricle in parietal temporal region.

no Babinski. The left arm seemed weaker than the right. The patient was observed for several days. However, by March 10, 1940, the date before admission to the hospital, the patient had become disoriented, inactive, and stuporous. The left arm was weaker than the right. There was suggestive facial weakness on the left. The reflexes in the left arm and leg were more active than on the right. The pulse was 52, the blood pressure, 150/90. On March 11, 1940, a ventriculogram was done (Figs. 5 and 6) which demonstrated a definite lesion in the right frontal area. A right frontal flap was turned. An enormous subdural hematoma extending from the parietal lobe to the tip of the frontal lobe was removed with a suction tip. This exposed an area of clot protruding through the tip of the frontal lobe. When

the clot was removed, there was a gush of old black blood from the subcortical area of the frontal lobe. Because of the fact that the frontal lobe gave the appearance of tumor, a right frontal lobectomy was done with removal of the frontal lobe anterior to the motor cortex. The wound was closed in the usual manner without drainage. The patient left the hospital on April 13, 1940, after a somewhat prolonged convalescence. This patient is now able to be up and about her home and is gradually regaining use of her left arm.

CASE 6.—M. K., aged 30 years, was admitted to St. Luke's Hospital on Aug. 6, 1940, with a chief complaint of paralysis of the right side of four days' duration. Four days before entry to the hospital, the patient had a gastrointestinal upset, consisting of nausea, vomiting, and diarrhea. He slept well that night and arose as usual the following morning. About 10 A.M. the mother found him lying on his bed in a stuporous condition, unable to talk or to move his right side. This condition

Fig. 8.—Case 6 (M. K.). Posteroanterior view. Entire ventricular system shifted to right.

continued without change until entry to the hospital. Physical examination showed: blood pressure, 108/74; temperature, normal; pulse, 54; respiration, 20. Neurologic examination showed a right central facial paralysis; the fundi were negative upon admission, but within three days had developed a slight hemorrhage about the left optic disk. There was some anesthesia of the face on the right and complete paralysis of the right hand and foot. The reflexes were decreased on right side and there was a right Babinski. There was a motor and sensory aphasia. Visual fields could not be obtained. It was thought the patient had a subcortical clot on the left side. On Aug. 8, 1940, a ventriculogram was done (Figs. 7 and 8), demonstrating a lesion in the left temporal parietal area. On Aug. 10, 1940, a left temporal parietal flap was turned in the usual manner. A needle was inserted behind the

Rolandic artery and above the Sylvian fissure to a depth of 5 cm., where a blood clot was encountered. The cortex was then split and a large clot exposed and removed with suction. Bleeding points were coagulated; the wound was closed without drainage. The patient's postoperative course was entirely normal for the first twenty-four hours, but he died suddenly on the second postoperative day and postmortem was refused.

METHODS OF TREATMENT

A ventriculogram was done in 5 of my cases with no untoward results and with invaluable aid as to correct localization of the clot. An encephalogram was unsatisfactory in the sixth case. Furthermore, the simple procedure of ventriculography introduces little hazard in the patient with intracerebral bleeding. Neurologic examination, be it ever so complete and suggestive, is not sufficient.

Two operative procedures have been used in the patients reported by the various authors. These are: a burr hole, with needling of the suspected area and evacuation of the old blood or clot; and an osteoplastic flap raised, with complete exploration of the diseased area demonstrated by ventriculogram.

The latter procedure is the one which I endorse and advocate. I do so for the following reasons: adequate exposure, complete control of bleeding, and removal of all macerated brain tissue. The wound is then closed without drainage.

COMMENT

In comparative analysis of the symptoms of my 6 cases, I find considerable similarity to those which have been abstracted from the literature. The predominant features to be remembered are headaches, dimness of vision or other visual symptoms associated with hemiplegia, and papilledema. When this group of findings is present, subcortical bleeding with clot formation must be considered in the differential diagnosis. It is interesting to note that, of the 23 cases analyzed, a diagnosis of brain tumor was made in 12 instances. Hemorrhage with clot formation was diagnosed in 4 and no preoperative diagnosis was given in the remaining 7 cases.

SUMMARY AND CONCLUSIONS

1. Six cases of spontaneous subcortical bleeding with clot formation are reported with operative intervention.

2. Accurate localization of the lesion by ventriculography is a necessity in these patients.

3. Complete exposure of the diseased area by an osteoplastic flap for the removal of clot, macerated tissue, and control of bleeding is very essential.

4. Aspiration of the clot through perforator openings is to be discouraged.

5. While it is difficult to make a diagnosis in these patients, the chief difficulty seems to be that the diagnosis is not usually considered.

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THE DIAGNOSIS AND TREATMENT OF SUBDURAL HEMATOMAS

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INTRODUCTION

INTRACRANIAL hemorrhage due to trauma is as old as trauma itself. As soon as our ancestors began to fall out of trees and to hit each other on the head with stones or clubs they undoubtedly began to have traumatic intracranial hemorrhages. This paper deals with traumatic subdural hemorrhage; that is, the accumulation of blood in the subdural space; and it includes a series of thirty-five consecutive cases operated on by me.

Subdural hematoma was familiar to the pathologist long before the surgeon began to treat it. Johannes Wepfer (1657) has been given credit for the first authentic description of this condition. D'Enrico and German quote him as finding at necropsy a large blood-filled cyst beneath the dura of a patient who had died after an "apoplectic stroke." Virchow's paper in 1857 on the subject was accepted as the final word for many years and consequently generations of pathologists and many surgeons as well considered subdural hematomas to be spontaneous in origin and designated them as pachymeningitis hemorrhagica interna. In 1914 Trotter took issue with this view and in an article which can hardly be improved upon twenty-six years later stated that the condition was post-traumatic and that the source of the hemorrhage was rupture of one of the superior cerebral veins as it traversed the subarachnoid and subdural spaces to enter a dural lacuna. He reported four cases with two deaths. The two deaths were in cases with bilateral hematomas and in both cases the brain failed to expand after evacuation of the clots, a complication that is still exceedingly troublesome to the surgeon. However, this single article could not offset the tremendous weight of Virchow's opinion and the subject of subdural hematoma was still closed until Putnam and Cushing published their study in 1925. They attempted to differentiate between the reactive or traumatic and the spontaneous hematomas, but they were forced to admit that the histologic differences seen in the membranes of the two types were only slight. In this paper only the traumatic subdural hematomas are considered as they are the ones that primarily interest the surgeon. The spontaneous ones are usually associated with systemic disease, blood dyscrasias, or carcinomatosis or sarcomatosis of the dura (Russell and Cairns) and seldom come to the attention of the surgeon. It is only

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necessary to add that the origin of traumatic subdural bleeding may be not only from rupture of superior cerebral veins (Trotter), but also from inferior cerebral veins which enter the sphenoparietal sinus, veins which enter the lateral sinus from the posterior or inferior surface of the temporal lobe, and at times, even from anomalous cerebral veins that may enter the dura from the convexity of the hemisphere.

CLASSIFICATION

The classification of subdural accumulations of blood or fluid has been troublesome and there is little agreement. These accumulations range from fresh fluid or soft blood clots to encapsulated collections of bile-colored fluid and even to accumulations (nonencapsulated) of xanthochromic fluid in the subdural space (subdural hydroma). Cases of the latter are not included in this report.

Leary classified subdural hematomas under five heads: (1) fresh fluid or soft clots, (2) firm clots, (3) chocolate-colored fluid with a neomembrane on the dural side, (4) chocolate-colored fluid enclosed in a double membrane, and (5) a fused double subdural neomembrane with absorption of the previously enclosed clot. These various stages do occur, but, for practical surgical purposes, the classification into acute and chronic types suffices. Some surgeons have questioned the rationale of dividing the traumatic subdural hematomas into acute and chronic groups since it is now generally recognized that they are all varying stages of the same lesion. I believe that there is ample clinical justification for this. The acute subdural clots are usually associated with brain injury, are relatively large to begin with, follow severe head trauma, and have a correspondingly high mortality. From a diagnostic standpoint they are to be differentiated from cases of localized brain injury and extradural hematoma. The chronic subdural hematomas usually are not associated with severe brain injury, or the patient has recovered from his brain injury; the clots are primarily small; they often follow slight trauma; and, if the condition is recognized before increased intracranial pressure has placed the patient in too precarious a state, the mortality is low. They have to be differentiated from slowly expanding lesions; e.g., tumor or abscess.

Chronic subdural hematoma has received by far the most attention in the literature. Out of fifty-five articles reviewed in the course of preparation of this paper, only six mention acute subdural hematoma. In the neurosurgical clinics the greatest experience has been with chronic subdural hematoma. Only in large emergency services has there been much experience with the acute types.

Great interest has been attached to the formation of the chronic subdural hematoma. It must be emphasized that these clots, even when solid or semisolid, show no lamellation or other evidence of repeated hemorrhages. It is probable that in only rare cases does repeated hemor-

rhage occur from either the original torn vessel or from the vessels of the capsule or neomembrane. The early clots are never encapsulated, which speaks against a possible intradural origin, as does the fact that, in successive stages of the formation of a neomembrane, it is always formed first on the dural side and that in old cases only does the neomembrane on the arachnoid side equal in development that on the dural side.

There is considerable variation in individual cases in the rapidity with which a neomembrane is formed. On the one extreme I have seen fairly well developed neomembranes within seven days after the injury that presumably caused the original hemorrhage; on the other extreme I have seen little evidence of neomembranes and semisolid clots as long as six weeks after the injury. In both cases the history appeared dependable.

Gardner, Zollinger and Gross, and Munro have developed the modern theory of the development of the large chronic subdural hematoma from a relatively small initial clot in the subdural space by the absorption of cerebrospinal fluid into the clot by osmosis. At first there is an equalization of osmotic pressure with the whole blood of the clot. As hemolysis of the whole blood takes place, the process is tremendously accelerated by the resultant great increase in osmotic pressure following the breakdown of large protein molecules.

DIAGNOSIS

The two sexes seem equally disposed to the development of these clots, although the greater frequency of head injury in the male makes them more frequent in that sex. In my series there were 26 in males and 9 in females. They were distributed between the ages of 20 and 70 years, although most of the cases occurred in the fifth decade. Age is an important factor in survival; there were only 3 survivals in the 10 cases occuring in the sixth and seventh decades of life (Table I).

The recognition of the acute subdural hematoma to a considerable extent parallels that of the extradural hematoma. Preoperatively it is often difficult, if not impossible, to differentiate the two, although typically the extradural clot gives an earlier onset of symptoms because it is usually due to arterial bleeding. The recognition of both depends essentially on the progression of symptoms. Of all the symptoms that may be produced by a developing hematoma, alteration of the state of consciousness is the most significant. Often restlessness and delirium in previously quiet and rational patients are the first signs of a developing hematoma. When initial injury to the brain has been slight there will be the classic "lucid interval" between the injury and the time the clot develops sufficiently to cause stupor or coma. In most cases of acute subdural hematoma there is severe initial injury to the brain and consciousness is never regained. Only the deepening of stupor or coma indicates the development of the hematoma.

Dilation of the homolateral pupil is one of the most dependable localizing signs of a hematoma in my experience, and, in addition, is a valuable sign of a developing clot when it appears after the patient has come under observation. If present at the time of admission to the hospital, it usually means localized brain injury. Thirteen patients in the series had a unilateral dilation of the pupil and in 12 dilation was homolateral to the clot. Of these 13 cases, nine were chronic and four were acute hematomas. The 1 case in which the dilation of the pupil was contralateral to the clot was in an acute hematoma. The exploration was unilateral and there may have been brain injury or another hematoma on the side of the dilated pupil. The patient lived two weeks. Death was thought to be due to pulmonary complications. Unfortunately necropsy was not performed.

Convulsions, if Jacksonian, are of great localizing value and usually indicate a hematoma, either extra- or subdural, although they may result from localized cerebral contusion or edema. They were present in 4 cases. Weakness or paralysis of the extremities with abnormal or pathologic reflexes is usually contralateral to the lesion; occasionally with a large hematoma, the contralateral crus cerebri is pressed against the free edge of the incisura tentorii and hemiparesis and pyramidal tract signs are produced homolateral to the clot. The presence of hemiparesis or signs of unilateral involvement of the pyramidal tracts, especially if progressive, is strong presumptive evidence of a hematoma, but it, too, may may be produced by localized brain injury. This finding was present in 19 of the 35 cases; it was contralateral to the clot in 13, homolateral in 6. The combination of homolateral dilation of the pupil and homolateral hemiparesis was seen in 2 patients; 1 had an acute hematoma, the other, a chronic. Localizing neurologic signs of some type were present in 24 of the 35 patients.

A slow pulse rate indicates the compensatory action of the cardiovascular center in response to increased intracranial pressure. Typically, the blood pressure will rise with the fall in pulse rate and an abnormally high pulse pressure will be present. It is helpful to record graphically the systolic and diastolic pressures and the pulse rate on the same chart. When compensation begins to fail, the pulse rate will rise and the systolic pressure will fall. When these two lines cross, the condition of the patient is usually precarious and the peripheral circulation is inadequate. The systolic pressure always falls more rapidly than the diastolic and the pulse pressure consequently rapidly becomes progressively lower. A high body temperature is another dependable sign of dangerously high intracranial pressure, as is an irregular respiratory rate, although this latter is so variable that it is difficult to make definite statements about it.

It is evident that any or all of the phenomena discussed in the foregoing paragraphs may be caused by localized cerebral injury (lacera-

tions, contusions, or even edema) and consequently are not diagnostic of a hematoma. However, it is rare to meet with an acute hematoma, epidural or subdural, that does not give one or more of these symptoms.

Symptoms of a chronic subdural hematoma do not appear for days or weeks, some times even months, after the original injury which may be forgotten either because of its apparent insignificance or because the patient has so completely recovered from its effects. The clinical picture is usually progressive. Mental disturbances often predominate and many of these patients are considered to be suffering from a psychosis. Headache and vomiting are often present and objective evidence of increased intracranial pressure in the shape of papilledema is often present. Record of a fundus examination was made in all but 2 cases of the series. Papilledema was present in 14 patients. All had chronic hematomas.

The spinal fluid was examined in 26 patients. Five of these had acute subdural hematomas; in all of them the fluid was blood tinged. In the 21 patients with chronic hematomas in which the fluid was examined, it was xanthochromic in 16. No examination of the spinal fluid was made in 4 patients with acute and 5 with chronic hematomas.

Air studies were made in only 1 patient in the series. This man had a choked disk, gave no history of injury, and had no localizing signs. Ventriculography revealed evidence of a space-occupying lesion in the right frontal lobe. Craniotomy exposed a small chronic subdural hematoma over the right frontal lobe. The openings in the parieto-occipital regions for ventriculography had failed to reveal the small hematoma. The patient later recalled several minor head traumas in the preceding six months.

TREATMENT

The methods employed by surgeons in dealing with these cases have ranged from large osteoplastic flaps to simple drainage through burr holes as originally and independently advised by Fleming and Jones and McKenzie in 1932. In only two cases in the present series has an osteoplastic flap been reflected. One has already been referred to; the case in which ventriculography was performed. In the other, because of the failure of the patient to rally after drainage of a large, well-encapsulated clot, an osteoplastic flap was reflected nine days later and the entire capsule meticulously removed. In spite of this, death occurred two days after this procedure. I feel this failure was due not to retention of the membranes of the clot after simple burr-hole drainage, but rather to failure of the brain to expand to occupy the space previously occupied by the clot. This point will be discussed further a little later.

Our practice when a subdural hematoma is suspected is to make a small (4 cm.) vertical scalp incision in the midparietal region above the ear, and after retraction of the scalp with a small self-retaining retractor, to make a burr hole just above the insertion of the temporal muscle. This can be done under local anesthesia in the great majority of cases.

If the patient is too restless or uncooperative for this, avertin may be used as a preliminary basal anesthetic.

If a subdural clot is present, this burr hole will reveal it in the great majority of cases. Since these clots are in the subdural space, of necessity they assume a pancakelike shape, spreading out over the surface of the hemisphere but being thickest at their point of origin. As we have pointed out, there are usually four possibilities for this origin. If the original bleeding has been from a superior cerebral vein, the clot's greatest mass will be toward the midline; if from an inferior cerebral vein entering the sphenoparietal sinus, the clot will be largely anterior and inferior. Clots arising from hemorrhage from veins passing from the posterior part of the temporal or occipital lobes to the lateral sinus will be predominantly posterior and inferior in location. Finally, those arising from tears in anomalous veins between the convexity of the hemisphere and the dura will have their greatest thickness over the convexity of the hemisphere.

If the case is an early one and an extradural hematoma is by chance present, this burr hole will likewise disclose it. The appearance of the dura can be depended on to reveal whether there is a subdural hematoma, as even fresh blood beneath the dura can be recognized by the abnormal darkening which it produces. It is my custom to enlarge the burr hole with rongeurs to a diameter of approximately 3 cm. before opening the dura if it is discolored. This opening is not in any sense a decompression, but does give room for such manipulations as are usually necessary.

After the dura is opened, the clot can be readily evacuated in the great majority of cases. If the clot is solid or semisolid, simple alternate irrigation with saline solution and suction through a catheter passed beneath the dura will serve to break it up. Irrigation with saline solution must be done cautiously or not at all in acute cases because of the swelling of the brain which it induces and which is often already present. In chronic cases there is often difficulty in getting the brain to expand and here repeated irrigations may be of value.

Occasionally, the primary burr hole may be near the edge of the clot; in such cases it is a simple matter to place another one over the center of the now localized clot. If the original burr hole does not reveal the clot and there is sufficient evidence, additional burr holes may be placed anteriorly and posteriorly. In all cases where a clot is not revealed on the suspected side, an exploration must be made on the opposite side. Failure to do this resulted in overlooking the clot in one patient in the series. Necropsy two days later revealed the clot on the opposite side. Attention has already been called to the frequency of false localizing signs in these cases. In this series homolateral hemiparesis or pyramidal tract signs were present in over 30 per cent of the cases that showed

such symptoms. Extracerebral space-occupying lesions would seem more likely to press the contralateral crus cerebri against the free edge of the tentorium.

Even when a clot is disclosed on the side first explored, it is wise in most cases to put a burr hole on the opposite side. Four patients in the present series had bilateral clots. In three cases both clots were discovered and evacuated at the original operation; all three patients recovered. In the fourth case the two explorations were a week apart. The second was undertaken because of the lack of satisfactory improvement after removal of the first clot. Death occurred from meningitis four days after the second operation.

In older individuals and especially in cases that come to the surgeon late, one occasionally finds that the cerebral hemisphere does not expand to fill the space formerly occupied by the clot. Trotter noted this in the two fatalities that he reported. Both Grant and Coleman in 1935 called attention to the grave prognostic value of this observation. Cohen reported a remarkable case of this type with final recovery after repeated aspirations of the subdural space. In my experience these cases all terminated fatally, in spite of drainage of the subdural space and postoperative intravenous administration of isotonic fluids in an attempt to swell the brain. Finally, at the suggestion of Dr. Jerry Kearns, I initiated a special technique for dealing with them. Now when at the operating table a brain fails to expand to occupy the space previously occupied by the clot after the clot has been thoroughly evacuated, the subdural space is filled with distilled water. A small tube drain is placed beneath the dura and the wound then closed in layers tightly about the tube. A clamp is placed on the tube, the head dressed, and the patient returned to bed. He is given 1,000 c.c. of distilled water intravenously followed by 1,000 c.c. of normal saline solution. The clamp is removed from the tube four to six hours later. This method was used in five such cases in the present series with four recoveries. In the patient that failed to recover, the technique was modified by the omission of the intravenous administration of distilled water; only normal saline solution was given intravenously. This patient followed the usual course of such cases in my past experience; he failed to rally, remained in coma, and died forty-eight hours later.

The danger of hemolysis following the intravenous administration of distilled water is obvious; in the four cases in which it was used, mild hemoglobinuria was noted for a day or two following the injection. However, no ill effects were noted clinically in any of the four cases. Its use is justified by the comparison of the previous poor result constantly encountered in this type of case with the success that this technique has met with.

In the case of either subdural clot or negative exploration, I like to place a drain of rubber tissue beneath the dura for twenty-four hours. It should not be left in place any longer but removed at the initial dressing the next day. This drain will take care of the slight oozing that may otherwise take place after the wound has been closed. More important is the provision for continuous supratentorial drainage of cerebrospinal fluid for the first twenty-four hours. This in itself may be of great help to the patient and has none of the dangers of lumbar drainage. The risk of infection is minimal and to my mind is offset by the advantages of drainage. These wounds are always closed in layers with interrupted silk sutures in the temporal muscles, fascia, galea, and skin.

SUMMARY OF CASES

The series of subdural hematomas reported here consists of 35 consecutive cases operated upon with a mortality of 43 per cent for the entire group. The mortality was 24 per cent for cases operated upon more than three days after the injury. Clots were removed in 34 cases. In 1 case, already referred to, the clot was not found on the side indicated by the neurologic findings and unfortunately the other side was not explored.

Nine of the 15 deaths were in cases operated upon within three days after the injury. Necropsy was performed by the coroner's physician in 5 of these cases; cerebral contusion or laceration was present in all. One of these cases has already been referred to; the patient with bilateral subdural clots who had two explorations a week apart and who succumbed to meningitis after the second exploration. Necropsy was performed in 5 of the 6 deaths occurring in cases operated upon more than three days after the injury. One of the patients, as already stated, had an unrecognized clot on the side opposite to that explored. The other 4 had pulmonary pathology of bronchopneumonia or lung abscess which was thought to be the immediate cause of death.

The cases are classified according to time elapsed between the injury and the date of operation in Table II. Here, of course, history at times may be unreliable. In Table III the hematomas are classified according to apparent age as judged by the appearance of the clot, the presence or absence of associated cerebral injury as disclosed at operation or

TABLE I

DECADE OF LIFE	LIVING	DEAD	TOTAL
3rd	4	1	5
4th	5	3	8
5th	8	4	12
6th	2	3	5
7th	1	4	5
Total	20	15	35

necropsy, and the size of the clot. In this table "acute type of clot" refers to solid, liquid, or semisolid fresh clots with no evidence of formation of neomembranes, even on the dural side.

It is evident from these tables that the mortality is very high in the acute or early subdural hematoma; that is, in unencapsulated clots operated upon within three days of the injury. These clots are often associated with cerebral injury, which is, I feel, the most important factor in

TABLE II

TIME BETWEEN INJURY AND OPERATION	LIVING	DEAD	TOTAL
1 to 3 days	1	9	10
4 to 14 days	8	2	10
Over 14 days	11	4	15
Total	20	15	35

the high mortality. Size of the clot is not so important, as the greatest mortality occurred in moderately sized clots. This group included most of the acute clots. As a result of my experience I have ceased operating upon the acute or early subdural hematoma except in those cases which are accidentally disclosed in the course of an exploration for an epidural hematoma.

TABLE III

	LIVING	DEAD	TOTAL
Acute type of clot	1	8	9
Chronic type of clot	19	7	26
Associated cerebral injury present	2	6	8
Associated cerebral injury absent	18	9	27
Clot up to 1 cm. in thickness	8	2	10
Clot 1 to 2 cm. in thickness	7	9	16
Clot over 2 cm. in thickness	5	4	9

CONCLUSIONS

In conclusion I would emphasize that acute, subacute, and chronic subdural hematomas are all progressive stages of the same lesion. Nevertheless, clinical differentiation can and should be made between the acute, or early, and chronic, or late, subdural hematoma. This differentiation is based on the early large size of the acute clots, their association with more or less extensive cerebral injury, and the high operative mortality.

The mortality is high in acute or early clots, in cases of associated cerebral injury, and in old people. Chronic or late subdural hematomas in young or middle-aged people without associated systemic disease have a good prognosis if operated upon before the effects of increased intracranial pressure have rendered the patient moribund.

Drainage through burr holes is satisfactory in the great majority of cases and subtemporal decompression or an osteoplastic flap is rarely necessary. In no case of death in this series was recurrence of the clot found at necropsy.

Bilateral exploration should always be done, especially if no clot is found on the side first explored. As already indicated, two deaths in this series are due to failure to observe this.

If, at the operating table, the brain does not expand to fill the space previously occupied by the clot that has been evacuated, special measures to induce expansion of the brain must be instituted. My particular procedure has been described.

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RECONSTRUCTIVE OTOPLASTY

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COMPLETE or partial reconstruction of the external ear has long been one of the major problems in plastic surgery. The chief stumbling block in rebuilding a new ear lies with the problem of furnishing an adequate support to the overlying skin. The numerous curves and levels of the normal ear cartilage make replacement of this tissue an important undertaking.

Prior to the following procedure the best attempt toward supplying a supporting framework consisted in the utilization of costal cartilage or a bone graft from the iliac crest that was shaped to represent the missing ear cartilage. Obviously neither source gave adequate material from which one could carve a structure that would closely represent the normal auricle, regardless of how adept the operator was as a sculptor. The most one could accomplish was to give the patient a poorly shaped rim or helix. The net result of such operative procedures was always disappointing, both to the operator and patient. Pierce,[1] Padgett,[2] and Kirkham[3] have revived the utilization of carved costal cartilage and, while their results are superior to those of their predecessors, several finer points are still lacking.

The use of any foreign material, whether it be metal, ivory, celluloid, or the like, is only to be mentioned because of the failures that result. Such material is not tolerated and like all foreign bodies is sooner or later extruded.

Before discussing plastic reconstruction it should be recalled that there appear to be only two tissues that can be successfully transplanted from one individual to another, namely cornea and cartilage. The success of transplant of these two tissues apparently is dependent upon the fact that neither has a blood supply and that they are kept alive by absorbing nutriment from adjacent soft tissues.

With the above in mind, we have been following the method recently devised by Gillies,[4] where an ear cartilage taken from another individual is used. The donor has always been and should always be a woman, who can cover the donor ear with her hair.

Since external ear defects commonly occur in children, the patient's mother is usually chosen as the cartilage donor. There is no special reason for choosing the mother except that she is invariably willing to do this for her child and thus the availability of an ear cartilage becomes more simplified.

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After preliminary surgical preparation, an impression of the donor's ear is first cast with warm, sterile dental modeling compound (Fig. 1). When hard it is removed and temporarily laid to one side.

To remove the cartilage, an incision is made along the posterior rim of the helix, exposing either all of the cartilage or whatever part is needed. The skin is then dissected from the anterior and posterior aspects of the cartilage, during which time careful attention is paid not to fracture the cartilage or perforate the skin during the process. After being completely freed, it can now be removed easily. The incision in the donor's ear is then sutured. The previously prepared mold (Fig. 1)

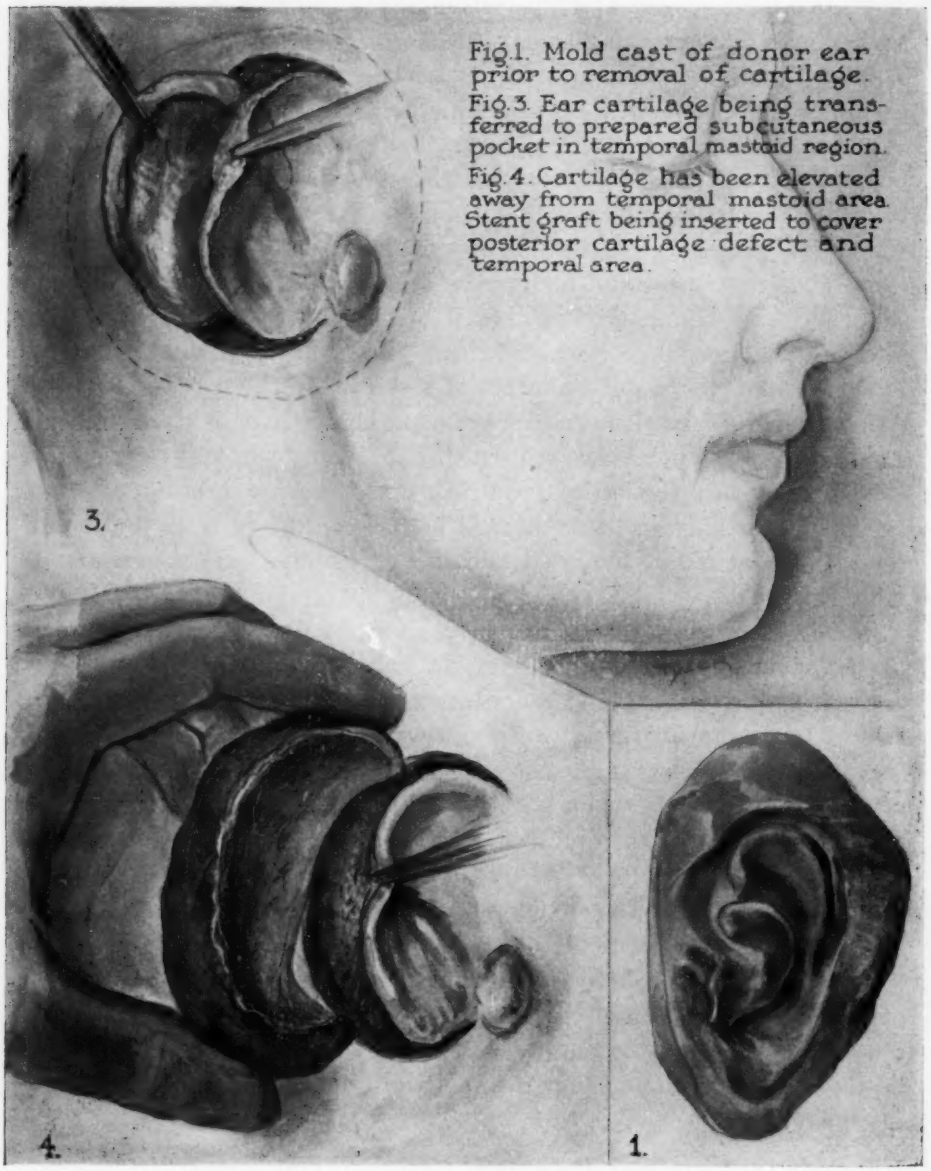
Fig. 1. Mold cast of donor ear prior to removal of cartilage.
Fig. 3. Ear cartilage being transferred to prepared subcutaneous pocket in temporal mastoid region.
Fig. 4. Cartilage has been elevated away from temporal mastoid area. Stent graft being inserted to cover posterior cartilage defect and temporal area.
3.
4.
1.

Figs. 1, 3, and 4.

is again placed upon the anterior aspect of the ear and secured by bandaging under moderate pressure. This procedure insures accurate coaptation of the two skin flaps. Although one may expect to have the completely unsupported ear tend to droop or shrivel, it is surprising how rigid they sometimes become due to the formation of a firm scar between the anterior and posterior skin coverings (Fig. 2). However, should any deformity occur, the donor can easily disguise this with her hair. The sacrifice is not, however, nearly as mutilating as one might suspect.

Fig. 2.—Donor ear showing healed state after removal of cartilage.

A curved incision corresponding to the normal anatomical location of the helix is now made through the hairless skin overlying the temporal and mastoid areas of the recipient. The skin is mobilized by freely undermining in all directions. After completing hemostasis the ear cartilage is then passed through this incision and placed in a normal anatomical position, following which the skin wound is closed (Fig. 3). Pressure is then made over the newly placed cartilage with a moist sterile marine sponge, held in place by bandaging. Small bits of the sponge may be cut out to fill in accurately all the underlying depressions to insure adequate adherence to each of the various ridges and concavities.

In three to ten weeks it will be noted that the mastoid skin is firmly adherent to the anterior aspect of the newly transplanted cartilage. At this time the original incision may be reopened around the rim of the cartilage, leaving a broad pedicle attached anteriorly. The entire mass is then lifted forward until it stands as a normal ear, matching its fellow on the opposite side. There now exists what appears to be a normal

ear from in front, but with a skin defect overlying the mastoid process and on the posterior aspect of the cartilage. This area is now covered by a Stent graft.

A piece of sterile warm pliable dental modeling compound is next pressed into shape to fit the defect behind the ear and mastoid process. After this has been permitted to harden, it is removed and covered with one single thick split-skin graft; that is, one large enough to cover both the mastoid and posterior cartilage defects. This graft is then spread over the mold with the raw surface outward, following which it

Fig. 5. Fig. 6.

Figs. 5 and 6.—Results of illustrated case. Existing primary skin tab has been rotated downward to become new lobule.

is reinserted into the defect behind the ear (Fig. 4) and is secured in place by a pressure bandage. Approximately one week later the bandage is reopened, the Stent mold removed, and the excess graft trimmed away. An ear of normal appearance is now observed, the transplanted cartilage being lined on the anterior aspect by the former mastoid skin and on the posterior side and mastoid process by newly grafted skin (Fig. 6).

For reconstructing partial losses, obvious modifications of the steps described may be carried out.

In congenital defects there is frequently a small tab of skin that can be swung downward to become the new ear lobule. If this is absent, a small tube pedicle flap raised nearby will furnish sufficient skin for this purpose.

The question has been raised as to what is the better time in which to reconstruct these congenital defects. As with other congenital disorders the results on the whole are usually best when done at the earliest age that the child will stand operation and cooperate. While the surgical problem is easier during the teens, from the psychological standpoint it is wiser to have this defect repaired before the child becomes too conscious of his abnormality; that is, before school age. We are not certain to date whether this ear will grow at the same rate as the normal ear, but it apparently remains at approximately the same size so that, even though the ear may be slightly larger at first, it will eventually match the one on the other side.

The average layman (and doctor) always asks about the question of reconstruction of the external auditory canal when this is absent due to congenital anomaly. We very definitely feel that this should not be attempted unless coincidental deafness exists. This operation is difficult to perform and is apt to be unsuccessful even though the canal has been re-established, because of the problem of maintaining its patency. From the practical standpoint these children seem to hear as well from use of their normal ear, thus making this surgery unnecessary. In other words, we are dealing chiefly with a cosmetic problem; the functional aspect is ordinarily but of secondary importance.

In conclusion, the following thought should be remembered. Many physicians see individuals who have just lost all or part of an ear in an accident. If the lost portion is completely detached, suturing it in place holds very little promise of success even if done immediately after the accident. On the other hand, this portion should never be discarded, but the cartilage should be saved for future reconstruction. If it is not feasible to bury it under the mastoid skin at once, it may be sutured into a subcutaneous pocket in the abdominal wall until one is prepared to place it in its permanent location.

SUMMARY

An operative procedure as recently developed by Gillies for the permanent replacement of the external ear has been described and found to be uniformly superior to previous methods. The operation utilizes an ear cartilage taken from another individual as the basis of the reconstruction. Such an architectural form gives far better cosmetic results than former operative procedures.

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CHRONIC UNDERMINING BURROWING ULCER

Report of Case Treated by Local Applications of Sulfanilamide

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CHRONIC progressive ulcers present a definite clinical entity and respond poorly to the usual therapeutic procedures. Meleney[1, 2] has described two types, one a "symbiotic progressive gangrenous ulcer," with gangrene of the skin margin but without undermining or deep penetration. This type is caused by the symbiotic action of a microaerophilic nonhemolytic streptococcus and a *Staphylococcus aureus.* These ulcers usually follow drainage of an intra-abdominal abscess or thoracotomy. The involved skin presents three characteristic zones: the outer, a bright red; the middle, a dusky purple; and an inner, gangrenous. The second type Meleney refers to as "chronic undermining nongangrenous burrowing ulcer." Here the infection burrows into the deep tissues, but there is no gangrene of the skin. The ulcers originate around chronic sinuses, produce liquefaction of the subcutaneous fat and connective tissues, and result in undermining of the skin margins. Recently Meleney[3] stated: "Chronic undermining ulcer is not a symbiotic infection but caused simply and solely by the microaerophilic hemolytic streptococcus."

Other authors refer to chronic progressive ulcers under the general term of "phagedenic ulcers."[4, 5] Most investigators have confirmed Meleney's work concerning the presence of anaerobic streptococci.[6, 7] As one reviews the cases reported, the majority of them fall into one of these two clinical entities. Meleney has recently classified chronic undermining burrowing ulcers into three types: the postoperative, the lymph glandular, and the secondarily contaminated. On the basis of this classification the following case belongs to the lymph glandular type.

CASE REPORT

F. J., a 32-year-old white male, was first admitted to the University Hospitals on March 13, 1939. One year prior to admission he developed an infection on the dorsum of his right hand, followed by an axillary suppurative adenitis which was drained on seven occasions and resulted in multiple draining sinuses. On routine physical examination the systems were found to be essentially normal. There was marked induration of the axilla extending halfway between the anterior axillary fold and the sternum and down on the chest wall as far as the fourth rib. Serologic tests for syphilis and agglutination studies for undulant fever, typhoid, and tularemia were all negative. Cultures from the sinuses grew the microaerophilic beta-hemolytic streptococcus and some diphtheroids. Repeated bacteriologic and pathologic examinations were made for fungi and tuberculosis, but none were found. A wide excision of the sinus tracts was performed on the first admission. The wound was treated with alternating dressings saturated with Dakin's solution and normal saline solution. At the time of discharge, May 3, 1939, a granulating surface 8 cm.

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in diameter was present. The edges were epithelializing and it was thought that the wound would heal.

The patient was readmitted to the hospital on June 26, 1939. During his stay at home daily dry dressings were applied. The ulcer had increased in size, measuring 13 cm. in diameter. Its base was covered with dirty gray granulation tissue and the edges had become undermined. An aerobic beta-hemolytic streptococcus and a *Staphylococcus aureus* were isolated. No anaerobic cultures were made. Three days after entering the hospital the undermined skin edges were excised. During the following eleven weeks numerous methods were used in an attempt to obtain a clean granulating surface. Dakin's solution, potassium permanganate, zephrin, and azochloramide were all tried. Sulfanilamide was given orally for eight days in doses which maintained a blood sulfanilamide level of 6 to 10 mg. per cent. Some improvement was obtained and grafting was subsequently attempted on two occasions without success. He left the hospital Sept. 14, 1939, because of a death in his family, without any appreciable change in the wound.

His third admission was on Jan. 29, 1940. The ulcer had further increased in size, measuring 20 cm. in diameter. Undermining of the edges was marked. No strictly anaerobic organisms were found, but an aerobic beta-hemolytic streptococcus was found and we now believe that more diligent studies would have revealed that this organism was the microaerophilic beta-hemolytic streptococcus which was isolated on the first admission. A *Staphylococcus aureus* was also isolated. The patient had developed a secondary anemia and for this he was transfused and given general supportive treatment. Zinc peroxide* applied locally for one week was followed by beginning epithelialization at the wound edges, but there remained a large amount of purulent exudate. Skin grafting was again unsuccessful except for two small grafts which remained viable. Realizing that a beta-hemolytic streptococcus was the predominant organism, and hoping for some treatment that would improve the condition of the wound more rapidly, local applications of sulfanilamide were instituted. The wound was covered with powdered sulfanilamide, and a gauze dressing, moistened with distilled water, was applied. Crusts of dried exudate were removed daily and sulfanilamide applied. After three days the granulations were bright red and the exudate had decreased about 90 per cent. Epithelium started to grow in from the wound edges and the two grafts which had survived rapidly increased in size. Grafting was repeated using small Thiersch grafts. These were left dry for six hours and then a moist dressing of sulfanilamide solution was applied. The solution was freshly prepared by dissolving 10 Gm. of powdered sulfanilamide in 1 liter of near-boiling water. Eleven days after the final skin grafting the wound was completely epithelialized. A recent follow-up revealed that the patient has remained well.

When these progressive ulcers were first recognized, wide excision was advocated. This is often satisfactory in the cases classified as "symbiotic progressive gangrenous ulcer." However, in the group of "chronic undermining burrowing non-gangrenous ulcer," excision alone is not adequate. Holman[4] treated a small series with maggots. Innumerable antiseptic preparations have been tried without success. Meleney and Harvey[3] have stressed the fact that all preparations of zinc peroxide are not active and have shown that certain technical features of the application must be strictly followed. Other authors[6, 7] have confirmed the value of zinc peroxide.

*Merck's zinc peroxide was tested for use and found to be "active." The test was carried out by adding distilled water to the preparation. The supernatant fluid became clear and contained bubbles.

Sulfanilamide has been given orally in many types of wounds. Goodman[8] reported improvement in chronic ulcers on extremities culturing aerobic streptococci. Meleney and Harvey[3] used sulfanilamide alone and in conjunction with zinc peroxide. They concluded: "It is possible for sulfanilamide [oral] to result in the healing of certain of these ulcers without the local use of zinc peroxide. However, the process of healing was very much longer than in the cases treated with zinc peroxide alone or with a combination of the two forms of treatment."

Several authors have reported successful local use of sulfanilamide. Jensen and Johnsrud[9] found it effective in preventing infection of compound fractures. It has been found to be of value in treating chancroid.[10] Long[11] used the drug in treating chronically infected superficial lesions from which beta-hemolytic streptococci were isolated. Sinclair[12] applied the drug to infected tooth sockets.

It is not the purpose of this paper to refute the value of zinc peroxide in the treatment of chronic undermining burrowing ulcers, since many cases of this type have been successfully treated by this method. However, it is our desire to present a case in which the local application of sulfanilamide brought about a more rapid improvement than was obtained with zinc peroxide and subsequently enabled successful grafting.

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ABSCESS OF THE LUNG

Bronchopulmonary Segment, Basis for Clinical Localization

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In a previous paper[1] attention was called to the observation that lung abscess developed in and was confined to, in the early stages, anatomical pulmonary units which were named bronchopulmonary segments. It was also shown that these segments were essentially constant in form and position and, because of their relationship to bronchi, could be designated in bronchoscopic localization. In a later paper[2] the significance of bronchopulmonary segments in roentgenologic interpretation was indicated. The anatomical studies which were made of the bronchi of these segments were in complete agreement with the classical studies of Ewart.[3] The term bronchopulmonary segment was devised, not to suggest a new anatomical relationship, but to place emphasis on a clinical pathologic view. The necessity for such emphasis became apparent as evidence accumulated that localized pathologic processes, such as putrid lung abscesses, bronchiectasis, and gangrenous bronchopneumonia, evolved in bronchopulmonary segments.

In the surgical treatment of pulmonary abscess, accurate localization is of primary importance if the best results are to be obtained by drainage operations. With precise localization the operative procedure[4] is usually simple, consisting of a limited exposure at the site of contact of the abscess with the thoracic parietes and incision, through adhesions, of the abscess. The free pleural space and normal pulmonary tissue are not traversed in such a precise one-stage operation, and severe, and frequently fatal, putrid empyema is avoided and excellent results can be achieved. Without the knowledge of the exact site of the lesion, the free pleural space and the normal lung may be seriously infected at operation.

The purpose of this paper is to present the anatomical basis for the localization of lung abscess and the general approach to the problem used at Mt. Sinai Hospital. In this institution on the surgical service 104 cases[5] of acute putrid lung abscess have been operated upon with four deaths. Apart from questions of surgical technique, the excellent results which have been obtained and the low mortality are in large part ascribable to accurate localization.

Before describing in detail the basic principles of localization, a résumé will be given of certain constant anatomical characteristics of lung abscesses as observed over a period of about ten years in a series

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of over 350 acute, subacute, and chronic cases. Emphasis should be placed on the fact that the statements to be made apply only to putrid pulmonary abcesses of substantial size and not to small cortical or miliary abscesses, small localized empyemas resembling pulmonary abscess, or nonputrid collections of pus from various sources.

1. Lung abscesses always lie in the periphery of the lobe, their most superficial portion being within one-quarter or one-half inch of the surface. The superficial situation is due to the onset of the disease in the finer bronchioles[6] which lie in the periphery. During the process of coalescence of necrotic foci into an abscess, the narrow layer of pulmonary tissue between the cavity and the pleural surface collapses and becomes a thin shell of infected tissue.

2. The superficial situation of pulmonary abscesses means easy surgical accessibility. There are exceptions in which abscesses, although quite as superficial as those facing costal surfaces, face interlobar fissures, the diaphragm, or the mediastinum.

3. The visceral and parietal pleurae over the abscess are practically always adherent and thus shut off the free pleural cavity. In only five cases in the entire series were costal adhesions absent and these were the instances referred to in the preceding paragraph.

4. There are sites of predilection. The lower lobe apical segment was the seat of the abscess in 40 per cent of the cases.

5. The lung abscess always lies in direct line with certain large bronchi. These bronchi are quite constant in number and position and the direction of the bronchi determines the direction of flow of the infected material and the position of the lesion. The reason for this relationship between the large bronchi and the abscess cavity is apparently that a spray or flood of infected material involving most of the fine bronchial branches is necessary to form a surgical lung abscess. Involvement of only one or two of these fine bronchi apparently produces very small cortical suppurative lesions which cannot be drained surgically. The breakdown of most of the branches of a larger bronchus produces the relationship noted between a cavity and a bronchus. This relationship of bronchus to cavity is important because, with a knowledge of the position of the bronchi shown to be practically constant, the sites of surgical abscess formation are known. In fact, long before the series of abscesses was studied, the possible locations of these lesions could be accurately predicted.

The bronchi which determine the position of the lung abscess are constant in number and position and are named according to the portion of lung into which they extend.

The pulmonary parenchyma supplied by each of the above-pictured bronchi may be outlined by injecting a colored fluid into the bronchus while the lung is moderately inflated. Fig. 1 shows these bronchi and segments and their nomenclature.

The anatomy of the bronchi and pulmonary segments described above has been corroborated by Neil and his co-workers.[7] Also of much interest is the fact that these workers have been able to demonstrate each bronchopulmonary segment in vivo[8] by injecting lipiodol through a catheter into a single segment and x-raying the subject.

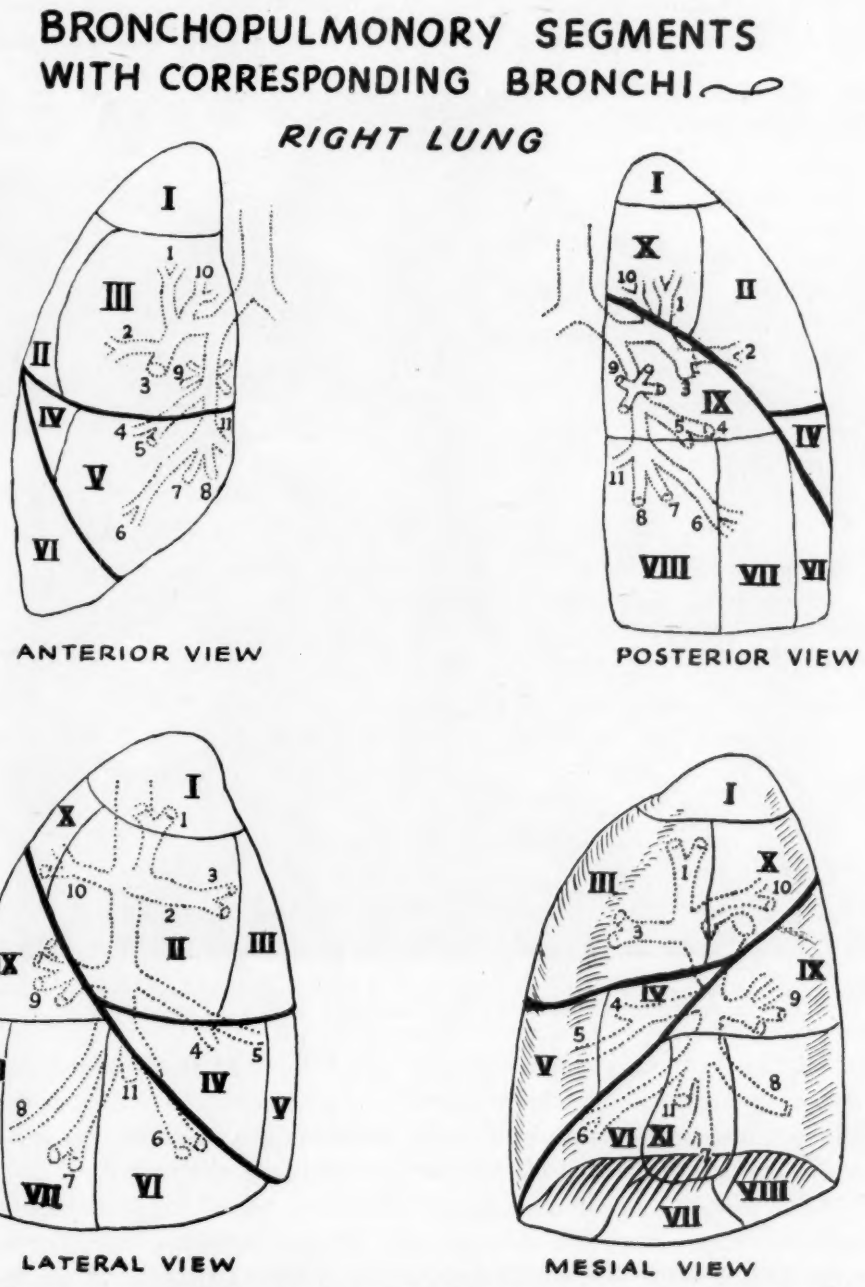

Fig. 1.—Arabic numerals identify bronchi and Roman numerals, their corresponding pulmonary segments in right lung. Left lung is the same except the mesial segment is rudimentary or absent. Upper lobe: Apical, *1*; anterior, *3*; axillary, *2*; paravertebral (upper), *10*. Middle lobe: Anterior, *5*; axillary, *4*. Lower lobe: Apical (middle paravertebral), *9*; paravertebral (lower), *8*; posterolateral, *7*; anterolateral, *6*; mesial, *11*.

The bronchopulmonary segments are constant in position, shape, and number. Anatomically they are useful in describing and locating parts of the lung. Pathologically they are units of disease processes, such as lung abscess, gangrenous and suppurative bronchopneumonia, and bronchiectasis. Each segment has a definite position in the thoracic cage and a definite location on roentgen film. The main bronchus of each segment has a characteristic direction which determines the position of an abscess

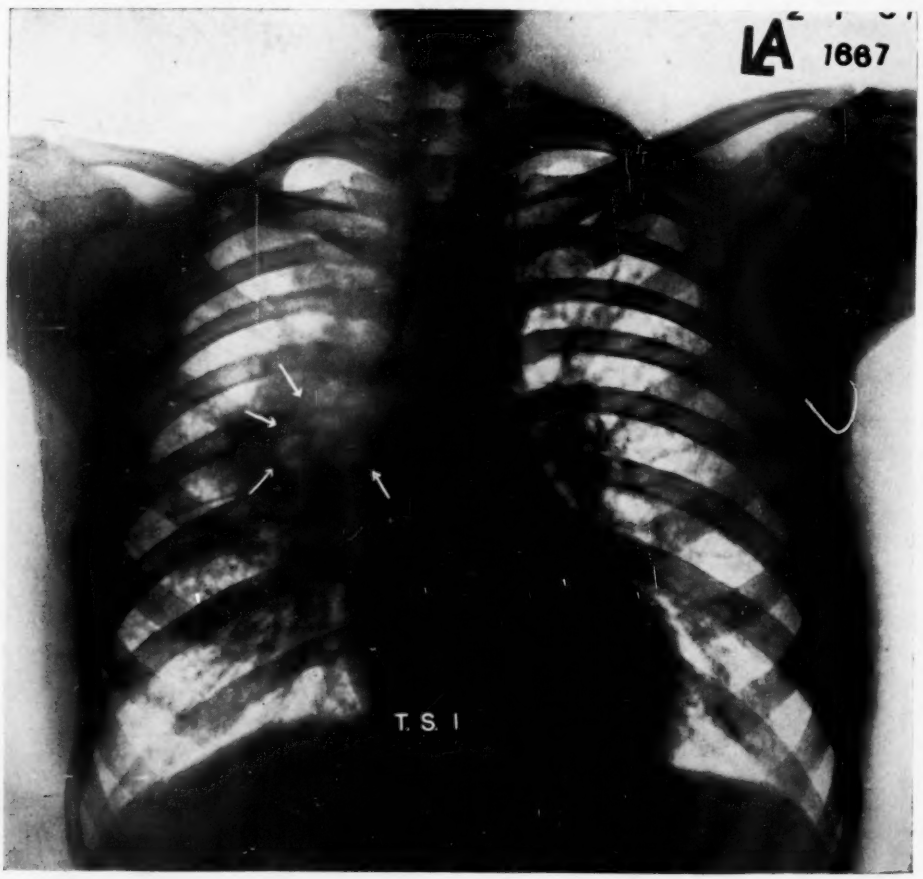

Fig. 2.—Posteroanterior plate showing lower lobe apical segment abscess (middle paravertebral abscess). This abscess must be drained posteriorly.

in relation to the costal surface; that is, whether the abscess lies next to the paravertebral, axillary, or anterior costal surface. On the roentgen film the inner field shadows are all posterior abscesses, except mesial ones. The lateral field shadows represent axillary abscesses.[2]

With this résumé of anatomical characteristics of lung abscesses in mind we may go on to a consideration of each bronchopulmonary segment as it is concerned in the localization of lung abscesses. A series of 100 consecutive cases of acute lung abscesses was analyzed to determine the location of the lesions according to segments.

Lower Lobe Apical Abscess (middle paravertebral abscess).—The most frequent site of acute lung abscess is the lower lobe apical segment. This portion of the lung lies halfway between the top and bottom of the lung field and borders on the mediastinum and vertebral column. The bronchus supplying this segment points backward and inward and so determines the site of the abscess cavity which is found under the costal surface next to the spine. Fig. 2 shows the position of the shadow of a lower lobe apical abscess on an anteroposterior x-ray plate. The exact site of drainage is determined by measuring outward from the spinous process of the vertebra and downward by counting the transverse processes beginning at the first thoracic. These abscesses are erroneously called central abscesses. Actually, such abscesses always lie immediately under the costal surface of the lung as described. Fig. 3, *IX* shows diagrammatically the position in the lung substance in lateral and anteroposterior views that a lower lobe apical segment abscess assumes. Forty per cent of all acute lung abscesses appear in this segment (right or left side), thus simplifying the problem of localization considerably.

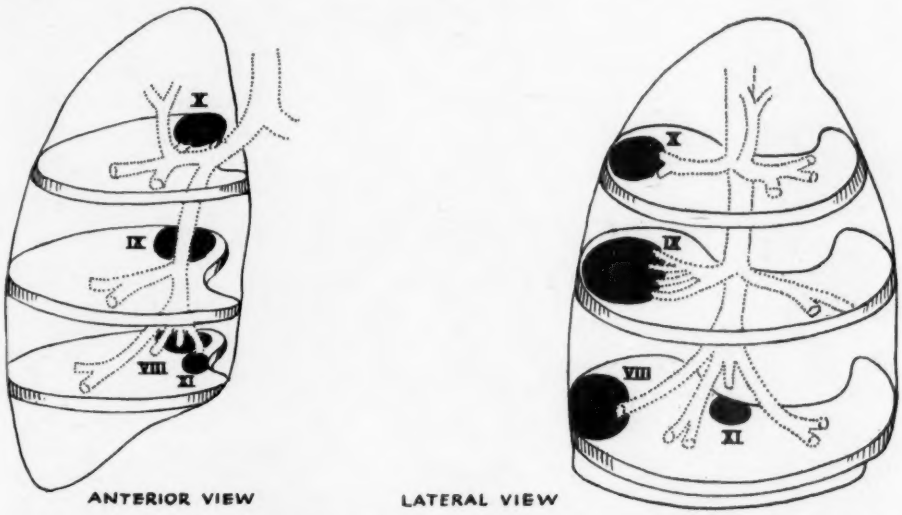

Fig. 3.—Right lung, anterior and lateral views. *IX*, Lower lobe apical segment (middle paravertebral) abscess; *X*, upper lobe paravertebral segment abscess; *VIII*, lower lobe paravertebral segment abscess; *XI*, mesial segment abscess.

Upper Lobe Paravertebral Segment Abscess.—Another frequent site of lung abscess is the upper lobe paravertebral segment. Fig. 1 shows the vertebral and costal surfaces and also the bronchus supplying this segment directed posteriorly and toward the vertebral column. This segment lies just above the lower lobe apical and the shadow of an abscess occupying this location lies in the upper part of the lung field next to the vertebral column (Fig. 4). The site of drainage is determined as in the previous segment and is usually about the level of the fourth thoracic transverse process. Eleven per cent of acute lung abscesses lie in this segment. Fig. 3, *X* shows diagrammatically the position in the lung

abscess, lateral and anteroposterior views, that an upper paravertebral segment assumes.

Lower Lobe Paravertebral Segment Abscess.—Continuing in the paravertebral region of the lung, we come to the lower lobe paravertebral segment. In addition to the paravertebral and costal surfaces, this segment has a diaphragmatic surface (Fig. 1). The bronchus supplying this segment is directed posteriorly downward and inward. Abscesses lying in this segment can always be reached directly through the posterior surface near to the vertebral column, although on rare occasions the pleural adhesions may be present only in the diaphragmatic surface. Six per cent of the cases lie in the lower lobe paravertebral pulmonary segment. Fig. 3, *VIII* shows the position that lower lobe paravertebral abscess assumes and Fig. 5 shows position on roentgenogram.

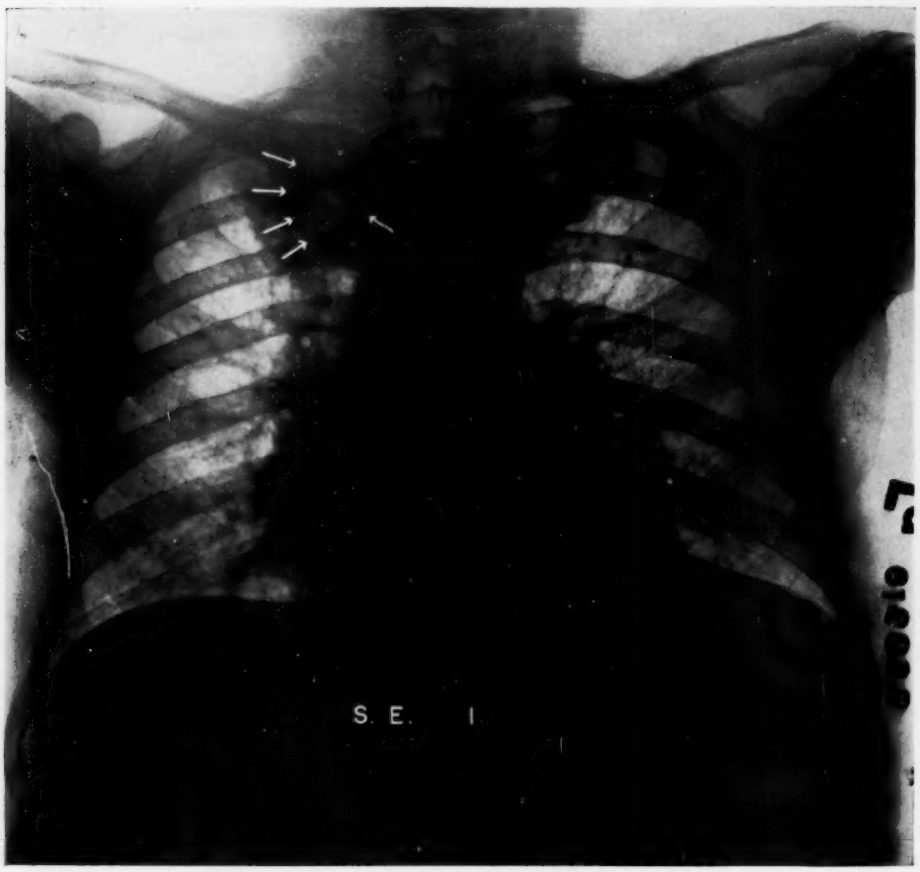

Fig. 4.—Position of upper paravertebral segment abscess in posteroanterior plate. This abscess must be drained posteriorly.

We see from preceding descriptions that the paravertebral segments, upper, middle, and lower, account for 57 per cent of all acute lung abscesses. These abscesses lie in the posterior part of the lung next to the vertebral column at the levels described and are represented on an an-

teroposterior x-ray by shadows lying in the medial lung field along the vertebral column shadow. Conversely, shadows lying along the vertebral column always represent abscesses in posterior segments. Lateral views always prove this, provided the abscess shadow can be distinguished from the bone of the vertebra.

The mesial segment (Fig. 3, *XI*) is the site of 3 per cent of the abscesses. This segment has only a mediastinal and diaphragmatic surface and its bronchus points downward. It lies halfway between the anteroposterior costal surface on the mediastinal aspect of the lung. This is the only site which cannot be drained directly through a costal surface

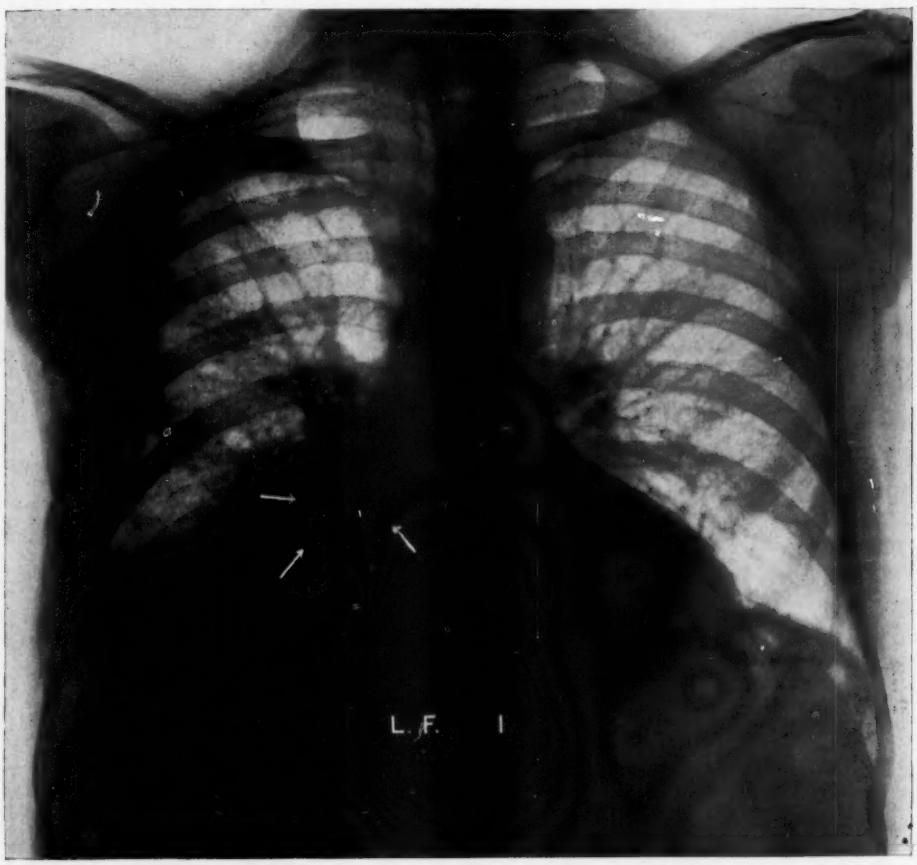

Fig. 5.—Lower lobe paravertebral abscess shadow. This abscess must be drained posteriorly.

and which requires a pushing aside of normal lung tissue in its drainage. It could conceivably, of course, be drained directly without traversing the free pleural cavity by incising upward through adhesions from the subdiaphragmatic space. So far this has not been attempted.

This abscess is about the same level as the lower lobe paravertebral abscesses, and at the medial part of the lung field the two sites cannot be distinguished in an anteroposterior x-ray and therefore require a

lateral x-ray for recognition. This will always show the mesial segment abscess shadow midway between the anteroposterior surface of the chest.

Lower Lobe Posterolateral and Anterolateral Segments.—The lower lobe posterolateral and anterolateral segments in addition to axillary surfaces have diaphragmatic surfaces where sometimes adhesions take place. Even though this is the case, the lesion is still very close to the costal surface (within one-half inch) and can be drained without traversing normal pulmonary tissue.

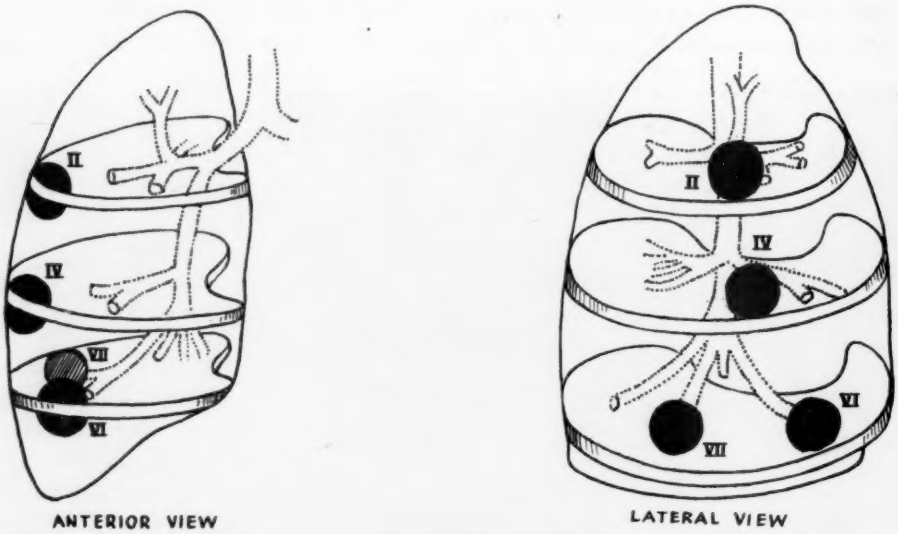

Fig. 6.—*II*, Upper lobe axillary; *IV*, middle lobe axillary; *VI*, anterolateral; *VII*, posterolateral.

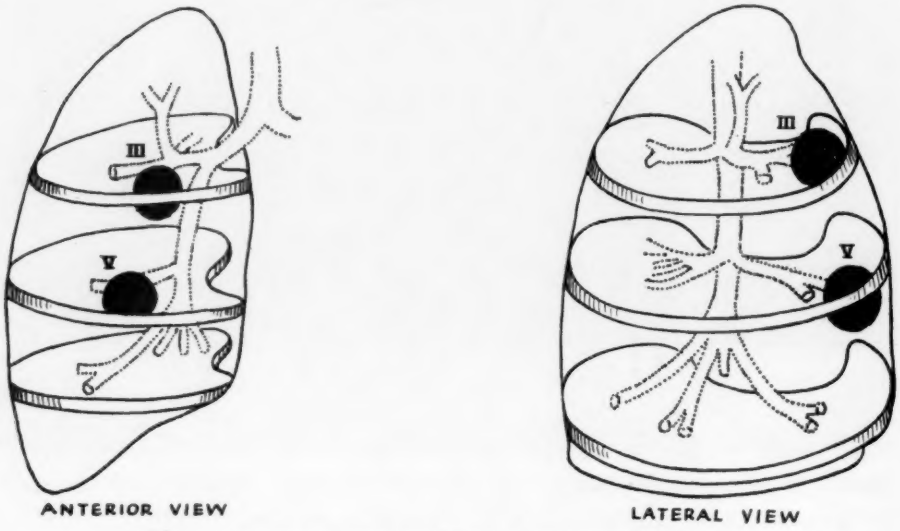

Fig. 7.—*III*, Upper lobe, anterior; *V*, middle lobe, anterior.

The lower lobe posterolateral is the site of 9 per cent of acute lung abscesses and the anterolateral segment is the site of 4 per cent (Fig. 6, *VI* and *VII*).

Middle Lobe Axillary and Anterior Segments.—These segments make up 3 and 2 per cent respectively of acute lung abscesses (Fig. 6, *IV*, and Fig. 7, *V*). The anterior segment in addition to an anterior surface has a mesial one. Since its bronchus is directed anterolaterally, the lung abscess always lies under its anterior surface next to the ribs.

Upper Lobe Anterior Segment.—This segment accounts for 3 per cent of the acute lung abscesses. As Fig. 8 shows, it has an anterior and mesial surface; but, since its main bronchus is directed anterolaterally, the abscess cavity is found under the anterior surface (Fig. 7, *III* and Fig. 8).

Fig. 8.—Upper lobe anterior segment abscess. Approach is anterior.

Upper Lobe Apical Segment.—This segment, lying as it does at the top of the lung, is rarely involved by aspirated infected material. In this series of 100 cases it has been involved in one instance.

Table I is a summary of the segmented sites of acute lung abscesses in 100 cases.

COMMENT

The situation of an acute lung abscess within the pulmonary parenchyma is dependent on the course and position of certain lobar

TABLE I

RIGHT LUNG		LEFT LUNG	
Upper lobe		Upper lobe	
Anterior	3		0
Axillary	11		7
Apical	1		0
Paravertebral	9		2
Middle lobe		Anterior descending	
Anterior	2		1
Axillary	2		0
Lower lobe		Lower lobe	
Apical	22		18
Paravertebral	3		3
Posterolateral	3		6
Anterolateral	3		1
Mesial	3		0
Total	62	Total	38

Summary

Lower lobe apical	(right and left)	40
Axillary	(right and left)	18
Anterolateral	(right and left)	4
Posterolateral	(right and left)	9
Upper lobe paravertebral	(right and left)	11
Lower lobe mesial	(right and left)	3
Lower lobe paravertebral	(right and left)	6
Middle lobe anterior	(right and left)	3
Middle lobe axillary	(right and left)	2
Upper lobe apical	(right and left)	1
Upper lobe anterior	(right and left)	3

bronchi which are anatomically constant. These bronchi, with their corresponding tissue, are designated as bronchopulmonary segments and are the lobar subdivisions on which the individual abscess is situated. Lung abscess occurs preponderantly in the paravertebral segments (57 per cent) and particularly in the middle paravertebral (lower lobe apical) segment (40 per cent). Gravity determines the segments most frequently involved. The lesion invariably is situated superficially within one of the lobes of the lung a short distance (within one-half inch) beneath the visceral pleura and usually facing the costal parietes. In the vast preponderance of cases the cavity can be entered directly through the overlying pleural adhesions and a thin shell of collapsed lung if the approach is made at the proper site. Lung abscess never lies in the center of the lobe and, if normal lung tissue is traversed in the surgical evacuation of the lesion, it must be concluded that the approach has not been made at the correct site.

SUMMARY AND CONCLUSION

1. The larger bronchi (subdivision of lobar bronchi) are constant in number and position.

2. The mass of pulmonary parenchyma aerated by each such subdivision has a constant shape, size, and position in the thoracic cage.

3. These bronchi with their corresponding parenchyma are known as bronchopulmonary segments.

4. The bronchopulmonary segments are units of clinical localization for lung abscess and other diseases due to aspiration such as bronchiectasis, bronchopneumonia, etc.

5. Bronchopulmonary segments are individually described.

6. A series of 100 cases of acute lung abscesses is analyzed according to bronchopulmonary segments involved and clinical location.

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SIMULTANEOUS BILATERAL SPONTANEOUS PNEUMOTHORAX

A Discussion of Its Mechanism and Report of a Case

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THE subject of bilateral pneumothorax has been repeatedly covered in the past. In the main, attention has been directed toward its incidence and its more frequent cause, viz., disease of the visceral pleura (Table I). It is the purpose of this communication to show that simultaneous bilateral spontaneous pneumothorax may follow operations not performed within the pleural cavity and may not be due to pleural disease. We will also discuss the mechanism of this type of spontaneous pneumothorax.

Oechsli and Miles[20] point out that instances of pneumothorax, excluding those that are traumatic and artificial, should be classified as spontaneous whether due to (1) some demonstrable pathologic change in the pleura which actually or presumably causes its perforation, (2) some cause that cannot be demonstrated, or (3) infection with a gas-producing organism. Olbrecht[21] reserves the term simultaneous bilateral spontaneous pneumothorax for those instances in which it occurs simultaneously or in which contralateral pneumothorax occurs before the original unilateral pneumothorax has disappeared.

The traumatic causes of pneumothorax, on the other hand, should be reserved for those cases where the injurious agent actually perforates the pleura. Such agents might be sword or bullet wounds, needle puncture, fracture of the rib, or direct forms of injury to the chest with disruption of the pleura. The cases we have collected from the literature and the one we are reporting represent instances of spontaneous pneumothorax that occurred without perforation of the pleura due to trauma or disease.

One mechanism by which spontaneous pneumothorax develops has been discussed by Sante,[25] Dorwart,[5] and Weinstein[27] and more recently demonstrated experimentally by Escudero and Adams.[8] In this type of spontaneous pneumothorax there is first partial atelectasis of a lung due to obstruction of a bronchus by mucus, such as may occur during or following anesthesia. If the diaphragm does not rise sufficiently, the mediastinum moves toward the affected side to neutralize the increased negative intrapleural pressure and the remaining lung becomes overexpanded. The pleura covering the now overdistended lung can rupture,

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TABLE I

DISTRIBUTION OF 82 CASES OF SIMULTANEOUS BILATERAL SPONTANEOUS PNEUMOTHORAX*

ETIOLOGICAL FACTOR	NO. OF CASES	APPROXIMATE PERCENTAGE
Pulmonary tuberculosis	39	48
Idiopathic	17	21
Emphysema	10	12
Pneumonoconiosis	7	9
Congenital cyst	3	3
Bronchopneumonia	2	2.5
Malignant tumor	2	2.5
Bronchiectasis	1	1
Interstitial fibrosis	1	1
Total	82	100

*From Glickman and Schlomovitz.[9]

producing a pneumothorax. Escudero and Adams[8] reproduced such a course of events in dogs and in one instance produced a bilateral pneumothorax. Curiously enough they also demonstrated that in dogs, when pneumothorax was induced on one side, the air could diffuse through the mediastinum and enter the contralateral cavity.

Eliason and McLaughlin[6] report 120 cases with pulmonary complications out of 7,326 operations. Of these 120 patients with pulmonary complications there was only one instance of pneumothorax, but the type of operation and the details of the complication are not discussed in the article. Although these figures may give a clue to the incidence of pneumothorax as a postoperative complication, it might be overlooked or it might be confused or diagnosed erroneously as postoperative atelectasis, which is by far a more common complication. The case described by Dorwart[5] and the one discussed by Weinstein[27] are illustrative of the latter possibility.

Dorwart's[5] patient was doing fairly well after the removal of a stone from the right kidney and a heminephrectomy. Suddenly on the eleventh postoperative day the patient became cyanotic and anxious, while the respirations jumped to 38 and the pulse to 160 without cough or pain. Twelve hours later a diagnosis of right massive pulmonary atelectasis was made, but thirty-six hours later, when x-ray films of the chest were made, a right pneumothorax was discovered. Without specific treatment the pneumothorax was absorbed and twenty days later the lung was completely expanded. An x-ray film of the chest taken two years after this incident showed that the lung fields were clear and without evidence of pulmonary tuberculosis. Dorwart[5] believes that the pneumothorax was preceded by a partial atelectasis of the lung which led to the pressure changes that produced a bursting of the remaining overexpanded lung with the consequent pneumothorax.

The case reported by Weinstein[27] was that of a 42-year-old woman who had a cholecystectomy with exploration and drainage of the

common duct. While reacting from anesthesia, she coughed considerably, became moderately cyanotic, and had a great deal of mucus in her pharynx. The cyanosis disappeared, but the cough persisted and subsequently dyspnea and cyanosis reappeared. Signs of partial atelectasis of the right lung were reported, but on the seventh postoperative day an x-ray of the chest showed a right pneumothorax with some mediastinal displacement to the left. The pneumothorax was slowly absorbed and eight weeks later on x-ray examination there was moderate thickening of the pleura. Weinstein[27] believes that the pneumothorax resulted from the rupture of a subpleural bleb.

The second mechanism has been demonstrated clinically by Keis,[16] Wiethe,[28] Iglauer,[11] and both clinically and experimentally by Champneys.[3] This mechanism has been either disregarded or lost sight of for some time, although in the thirteenth edition of Osler's *Principles and Practice of Medicine,* Christian[4] mentions Champneys' experimental work as illustrating a cause of mediastinal emphysema.

To test out the efficiency of various types of artificial respiration, Champneys[3] did experimental tracheotomies on twenty-one stillborn infants and then performed artificial respiration. Mediastinal emphysema was noted in seven instances and of these five had a pneumothorax. In one experiment the pneumothorax was bilateral. Champney noted that in six of these seven cases showing mediastinal emphysema there was a sucking sound heard at the base of the neck about the tracheotomy wound. By continuing his observations and using colored fluids he was able to trace their course down into the superior mediastinum. He postulated two conditions that must be present to favor the production of mediastinal emphysema. The first is a wound of the deep cervical fascia, and the second is obstruction of the air passages with continuation of forced inspiratory movements. If the pressure in the mediastinum is equalized by removing the obstruction in the air passages, the emphysema does not progress. However, if the obstruction is not removed or forced, inspiratory movements continue; i.e., there is a continued marked difference between the atmospheric mediastinal and intrapleural pressure, the mediastinal parietal pleura ruptures, and air from the emphysematous mediastinum diffuses through, producing a pneumothorax.

From the records of St. Bartholomew's Hospital, Champneys found three autopsied cases of mediastinal emphysema following tracheotomy. A unilateral pneumothorax was present in one and a bilateral pneumothorax was present in a second case. One of these cases had subcutaneous emphysema. From 1860 until 1884 the records of the Hospital for Sick Children yielded eighty-two cases with autopsies following tracheotomy for various causes. Mediastinal emphysema was present in five cases; one had bilateral pulmonary collapse, and three had subcutaneous emphysema, but none was recorded as having had a

pneumothorax. He believed that the pneumothorax was probably missed in many instances because it was not expected and it was not particularly looked for. In a later publication from the same hospital ten additional autopsied cases of mediastinal emphysema were reported following tracheotomy and in two pneumothorax was found.

The experiments performed on rabbits by Ballon and Francis[1] may be interpreted as offering confirmatory evidence of this principle. A rubber balloon was placed in the mediastinum of living rabbits and the effects of variations in the mediastinal pressure were noted. They observed that pneumothorax developed when the increased mediastinal pressure was greater than the mediastinum could withstand. They also showed that mediastinal emphysema may be a consequence of a pneumothorax or a pneumothorax may be due to what was originally a mediastinal emphysema.

The earliest cases of pneumothorax following a surgical procedure are those mentioned by Wilks and Moxon[29] in their Lectures on Pathological Anatomy, in 1875, referred to by Champneys. They described two cases as follows: "We believe we have seen two cases of pneumothorax arise from tracheotomy and we mention the circumstances because we are not aware that it has ever been alluded to. In one case, where after tracheotomy, death occurred without sufficient reason, both lungs were found contracted in the chest and the cellular tissue in the posterior mediastinum was filled with air producing large bubbles, which we think had burst the pleura into the chest. In another case where most extensive superficial emphysema followed the operation, the breathing became laborious before death, and the lungs were found contracted in the same manner; the emphysema having penetrated the mediastina."

Iglauer[11] reported a case of low tracheotomy in a 23-month-old child. He noted a marked sucking noise at the base of the neck. At the conclusion of the operation, subcutaneous emphysema was present and an x-ray of the chest disclosed an almost complete right-sided pneumothorax. In a similar vein Leiner[17] reported twelve cases of tracheotomy in children in nine of which mediastinal emphysema ensued, but there were no cases of pneumothorax. Crepitation synchronous with the cardiac systole was the chief sign observed. Eight of the cases had subcutaneous emphysema.

Wiethe[28] added two cases of left-sided pneumothorax in children following low tracheotomy. Both cases survived. He made further anatomical observations on post-mortem material, but his explanation of the mechanism of the pneumothorax was that of laceration of the left pleural dome during operation, thus favoring a traumatic cause for the pneumothorax.

Mediastinal emphysema with pneumothorax may follow thyroidectomy, particularly when substernal portions of the gland are removed.

Keis[16] describes a case in which a thyroid tumor was removed under general anesthesia. There was a period of dyspnea during the operation. Without further details Keis states that the patient died. Autopsy showed a mediastinal emphysema with bilateral pneumothorax. There was no demonstrable pleural injury or pulmonary disease. He collected seven other cases from the literature where mediastinal emphysema followed thyroidectomy. In four of these cases a bilateral pneumothorax was demonstrated at autopsy and no injury to the pleura was observed. From Keis' bibliography we have located three of these cases. Jehn and Niessen's[14] patient developed respiratory symptoms within one hour after the operation. Gold[10] reported four cases of mediastinal emphysema following thyroidectomy, one of which showed subcutaneous as well as bilateral pneumothorax. During the operation on this patient a hissing noise was heard at the base of the neck. Lotheisen's[18] case had malignant struma with severe tracheal stenosis. Five days after partial thyroidectomy, a tracheotomy was performed and a hissing sound of aspirated air was heard before the tracheotomy was completed.

Jessup[15] in a review of the subject of mediastinal emphysema lists six pathways in order of their frequency by which air may get into the mediastinum: (1) the pulmonary interstitial tissue extending along the peribronchial and perivascular connective tissue to the hilus, thence diffusing into the loose areolar tissue of the mediastinum; (2) extension of a subcutaneous emphysema along the endothoracic fascia at the jugulum; (3) the direct sucking of atmospheric air through wounds in the superior and inferior apertures of the thorax; (4) injury of the trachea and main bronchi whereby air is blown directly into the mediastinum; (5) openings in the mediastinal pleura so that air produced by pneumothorax is admitted; and (6) extension of retroperitoneal emphysema through the crus of the diaphragm.

The case reported by Phillips, Waldron, and Vanzant[23] may be illustrative of the sixth pathway mentioned above. The patient was a white male, aged 29 years. A subtotal gastric resection with Polya anastomosis was performed for perforating duodenal ulcer. The patient did not take the gas-ether anesthesia well and at the end of the operation there was noticeable subcutaneous emphysema in his neck with dyspnea and cyanosis. The emphysema continued to increase. On the next day a film of the chest showed a right partial pneumothorax. There was a stormy postoperative course with a good deal of coughing. A roentgenogram taken on the eleventh postoperative day showed a bilateral pneumothorax that was complete on the right and partial on the left.

The authors presume that there were bilateral emphysematous blebs and, following the strain of anesthesia, one of these ruptured on the right side, resulting in a pneumothorax which was accompanied by a passage of air up through the mediastinum into the neck and over the chest, producing the subcutaneous emphysema. The left pneumothorax

was attributed to the rupture of another emphysematous bleb from the postoperative coughing.

Although the above explanation may be correct, another mechanism is rupture of the diaphragmatic peritoneum with the development of mediastinal emphysema by aspiration of air through the crus of the diaphragm. Sufficient surgical injury to the retroperitoneal tissues may have occurred during the operation to permit the aspiration of air, particularly when it is considered that there had been respiratory difficulties during the operation. Similar cases have been reported in the literature. Ritter[24] described subcutaneous emphysema of the head and neck following excision of a gastric ulcer. Jessup[15] described a fatal case of mediastinal emphysema following splenectomy, during which the diaphragm was incised and repaired. No pneumothorax was observed at the autopsy. Newman[19] reported a case of generalized emphysema first appearing at the jugulum following a rupture of the stomach. Erichsen's patient[7] developed subcutaneous emphysema after the bladder had been punctured through the rectum for acute urinary retention, although from the clinical description one may assume that the patient may have had a gas bacillus infection. A similar case was reported by Tatum.[26] Pearce[22] described a case in which perforation of the esophagus was associated with an abscess of the cardiac end of the stomach. The patient died from subcutaneous and mediastinal emphysema with bilateral pleural effusion.

CASE REPORT

The case which we wish to present is that of a 57-year-old white male, a painter by occupation, who first applied at the Memorial Hospital Clinic on Sept. 28, 1938, at which time he complained of hoarseness and cough of sixteen months' duration. The family history was irrelevant. There was nothing in his past history suggesting antecedent pulmonary infection and there were no pulmonary symptoms suggestive of emphysema at the time of admission to the clinic. He was a heavy user of tobacco.

Physical examination disclosed a tumor of the left vocal cord with fixation of the structure. The remainder of the physical findings were within normal limits.

A biopsy of the left vocal cord was reported as epidermoid carcinoma, Grade II. Wassermann and Kahn tests were negative. Blood chemistry studies were within normal limits and a roentgenogram of the chest was normal.

Inasmuch as the lesion was limited to the intrinsic larynx a total laryngectomy was done on October 31, 1938, under local anesthesia. A permanent tracheal opening was left at the root of the neck in the midline.

Beyond a transitory pharyngeal fistula and low-grade cellulitis of the neck, the postoperative convalescence was uneventful. The patient was discharged on the fiftieth postoperative day.

Gross and microscopic studies corroborated the biopsy.

He remained free of disease until September, 1939, when a metastatic node was found in the lower left cervical region. He was readmitted to the hospital for a radical neck dissection. On Sept. 29, 1939, a radical neck dissection was done under local anesthesia. Due to the fact that the patient already had a tracheotomy, it was necessary to suture a tube in place in the tracheal stoma in order to cover

this area with sterile drapes. The dissection was carried out from below upward. The sternal and clavicular insertions of the sternocleidomastoid muscle were severed early in the operation and the internal jugular vein was taken along with the muscle. The metastatic node was removed with these structures. During this time the patient had no difficulty breathing. However, during the latter part of the operation when the dissection was being carried out in the upper portion of the left neck, the patient experienced gradually increasing dyspnea. Coincidentally, there

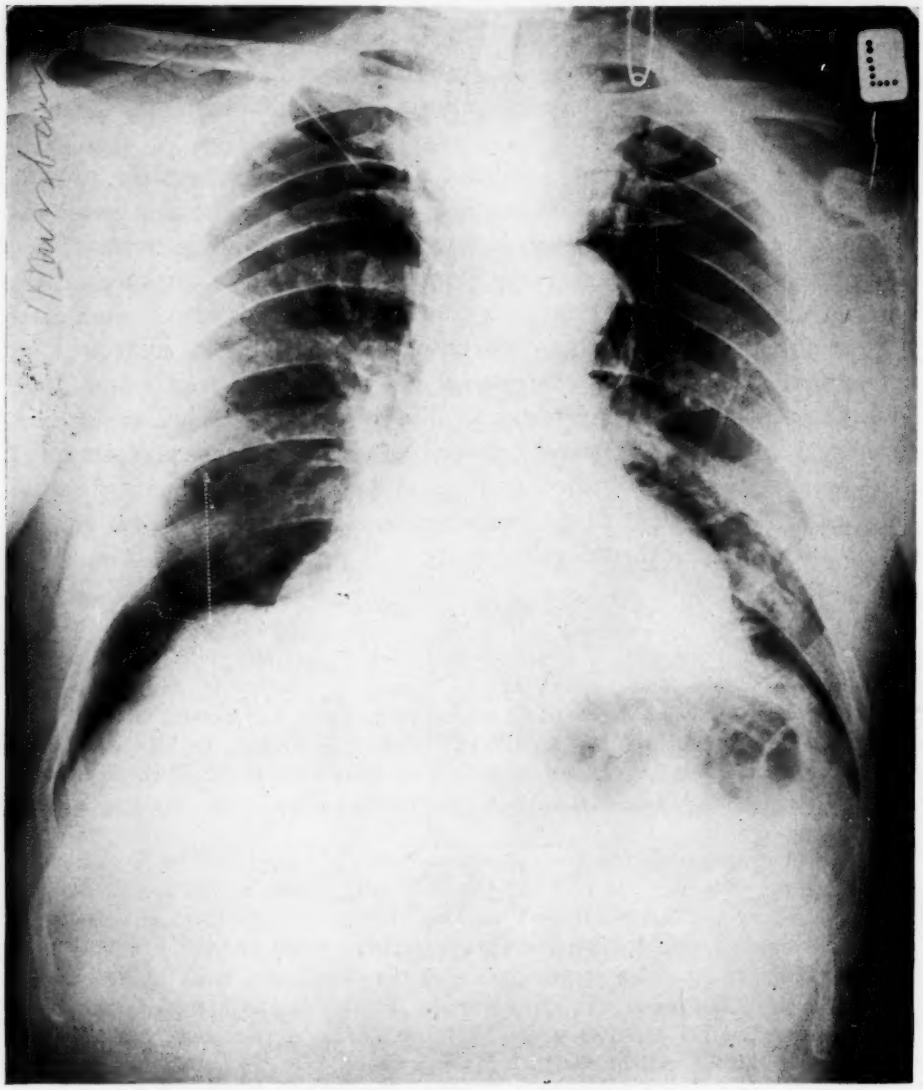

Fig. 1.—Sept. 30, 1939. Film showing bilateral pneumothorax. Apex and base involved in right side and apex involved in left side.

was a loud sucking noise heard in the left supraclavicular fossa and the tissues in this area alternately rose and fell with each respiratory excursion. Attempts to relieve the patient by rearranging the drapes and administering oxygen through the tube were only partially successful.

He was returned to the ward after the completion of the operation. At that time he was quite cyanotic and dyspneic with a respiratory rate of 30. Three hours postoperatively his condition was poor. He complained continually of a squeezing

pain in the lower sternal and epigastric areas and he was in mild collapse. There was moderate cyanosis despite the continuous administration of oxygen through the tracheotomy tube and his face was somewhat puffy. The respiratory excursions were increased in rate and depth. There was subcutaneous emphysema over the right upper anterior chest.

Percussion over the left hemithorax and right anterior chest showed hyper-resonance. Over the right posterior chest the note was tympanitic. The breath sounds were questionably audible over the upper four-fifths of the chest. Posteriorly at the bases there was a transverse bandlike area where the breath sounds were more easily heard but they were still distant. Expiration was prolonged.

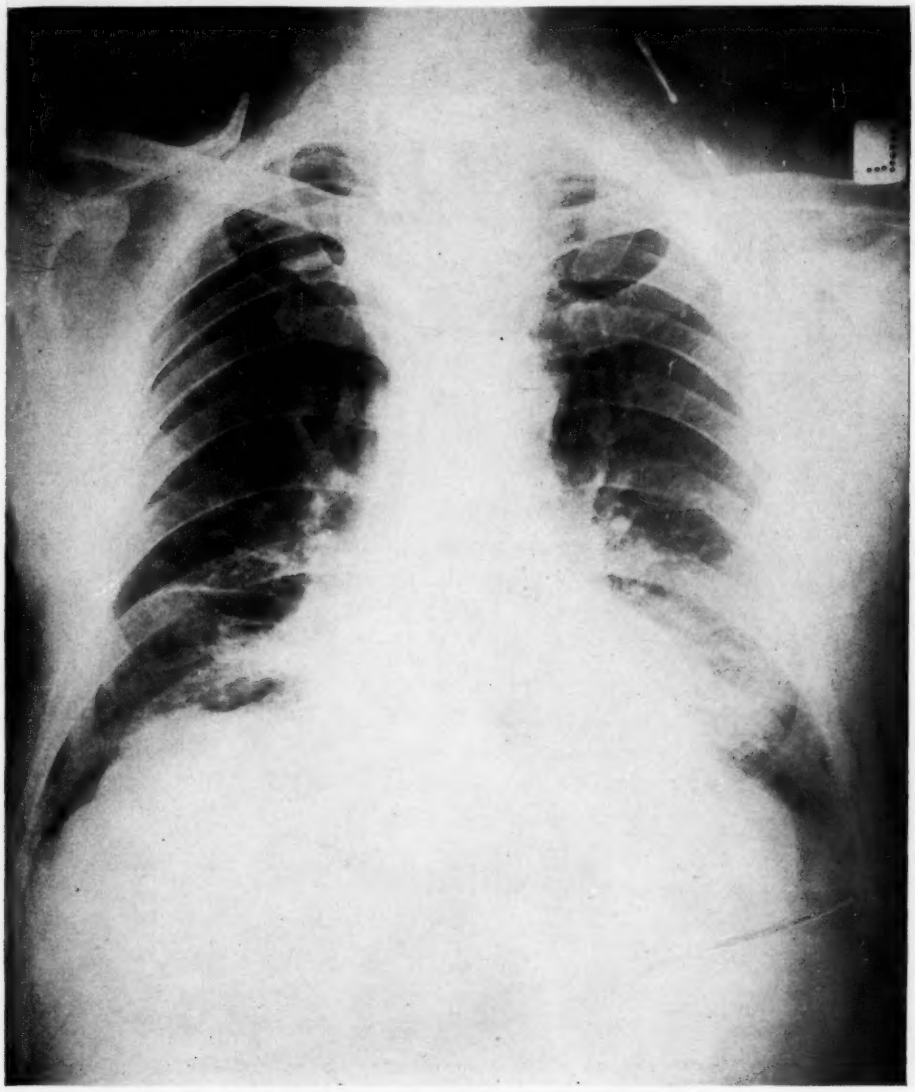

Fig. 2.—Oct. 9, 1939. Film of chest showing bilateral pneumonitis of lower lung fields. Pneumothorax has completely disappeared.

The pulse rate was 88 with occasional extrasystoles. The blood pressure was 128/80. The area of cardiac dullness was obscured by the hyper-resonance of the left chest. The heart sounds were barely audible and there was a faint crackling sound that was synchronous with each systole.

The abdomen was distended without tenderness or rigidity.

An electrocardiogram showed normal sinus rhythm, normal PR and QRS conduction time. There was no evidence of coronary occlusion.

A clinical diagnosis of bilateral spontaneous pneumothorax with mediastinal emphysema was made.

The patient was treated expectantly with supportive measures and in a few hours he was much more comfortable.

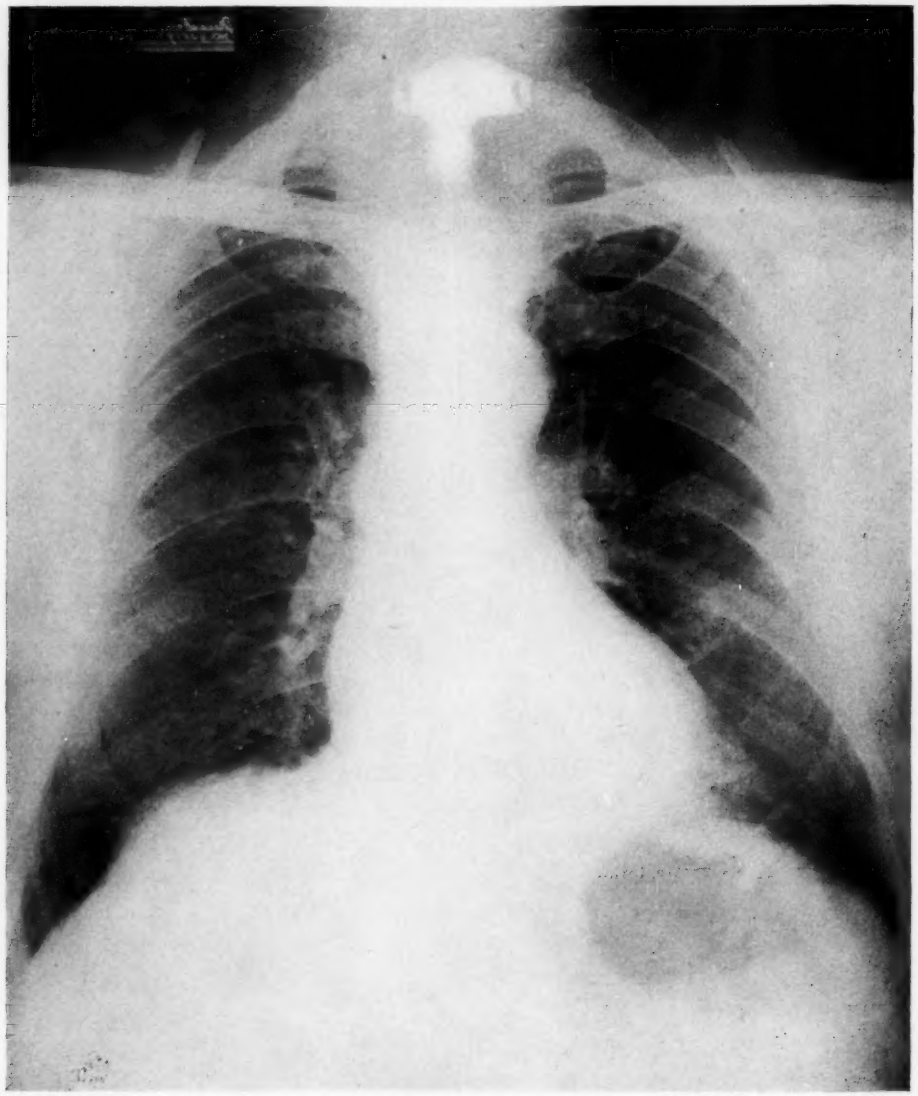

Fig. 3.—Oct. 19, 1939. Film showing return to normal.

The next morning, Sept. 30, 1939, there was clinical evidence of increasing expansion of both lungs at the bases, but no breath sounds were audible over the upper one-third of either lung field. At the same time a chest film showed a bilateral partial pneumothorax which was more marked on the right side than on the left (Fig. 1).

By Oct. 2, 1939, the patient was over the acute features entirely except for some mild hyperpnea. The subcutaneous emphysema increased moderately over the right anterior chest, but later it was gradually absorbed.

His convalescence was complicated by an erysipeloid infection of the wound and a bilateral pneumonitis of a mild degree (Fig. 2). By the twentieth postoperative day the patient was clinically well and a film of his chest showed no evidence of any abnormality (Fig. 3). He was discharged on the twenty-third postoperative day.

In December, 1939, the patient had a plastic operation for stenosis of the tracheal stoma. There were no complications associated with this operation. A month later there was no evidence of any effects from the pneumothorax which was completely absorbed. He has subsequently remained well.

In the consideration of the development of the pneumothorax of this patient there are several salient features which should be emphasized. First, there was the obvious difficulty of breathing with strong inspiratory efforts. This condition was accompanied by a loud sucking noise in the left supraclavicular fossa. Direct injury to the pleura might be regarded as the cause of the dyspnea and the pneumothorax, but it must be borne in mind that the symptoms and sucking sound first occurred toward the end of the operation when the dissection was being carried out on the upper part of the neck.

It would seem more likely that some partial mechanical obstruction to the patient's air supply occurred late in the operation, possibly through disarrangement of the drapes or compression of the oxygen supply tube. In either event, there was sufficient air hunger to produce dyspnea with strong inspiratory efforts. This corresponds to Champneys' first requirement for the development of mediastinal emphysema. A sucking noise was heard in the left supraclavicular fossa and this observation was also made in cases reported by Champneys,[3] Iglauer,[11] Wiethe,[28] Gold,[10] Lotheisen,[18] and Buford.[2] Wiethe points out that this sucking sound may be confused with aspiration of air into the veins and, in fact, such a complication was considered in the case which we have described. However, since hemostasis was complete in the lower cervical region, other causes for the noise were considered.

Champneys' second cause for the development of mediastinal emphysema, a wound in the deep cervical fascia, was more than fulfilled in this case, since a portion of the deep cervical fascia was removed with the specimen. We are thus of the opinion, in accordance with the experimental findings of Champneys, that, because of the violent inspiratory efforts of the patient, air was drawn into the mediastinum through the defect in the deep cervical fascia. The patient continued his inspiratory efforts for twenty minutes or longer. Apparently, sufficient difference in pressure between the mediastinum and pleural cavity resulted to permit the rupture of the mediastinal pleura on both sides with the production of a bilateral pneumothorax.

Besides the signs of bilateral pneumothorax the patient had subcutaneous emphysema. This was noted in cases reported by Wilks and Moxon,[29] Champneys,[3] Iglauer,[11] Gold,[10] Phillips, Waldron, and Vanzant,[23] and Buford.[2] However, subcutaneous emphysema without pneumothorax is not at all uncommon after operations about the root of the neck.

We also observed the sign emphasized by Leiner;[17] that is, a crackling sound synchronous with cardiac systole, supposedly indicative of mediastinal emphysema. It is conceivable that this could be produced by the contraction of the heart against a partially collapsed left lung.

The pain experienced by the patient was no more unusual than that seen in spontaneous pneumothorax resulting from other causes. Its location suggested the possibility of a coronary occlusion, but immediate and successive electrocardiograms failed to disclose any evidence of myocardial infarction. There were progressive changes noted in the electrocardiograms, but these can be explained by displacement and rotation of the heart with its subsequent return to its normal position. Buford's patient,[2] however, had mediastinal and subcutaneous emphysema following a thyroidectomy, but pneumothorax was not observed and no x-rays were taken. In addition, his patient had great precordial fullness and precordial pain with each inspiration. The symptoms were greatly accentuated by deep breathing, which was characteristic of our case. According to Jessup[15] the outstanding effect caused by mediastinal emphysema is a mechanical interference with circulation brought about by a compression of the large veins entering both sides of the heart. The clinical and experimental observations of Jehn[12] and Niessen[14] on mediastinal emphysema confirm this conclusion. A case is reported by Jehn[12, 13] in which the mediastinal emphysema was so great that very little blood was found in the cardiac circulation because of the compression of the great veins entering the heart.

We do not believe that this occurred in this case since there was no appreciable engorgement of the cervical or brachial veins and the electrocardiograms did not suggest myocardial anoxemia.

SUMMARY

A case is described of spontaneous bilateral pneumothorax accompanied by mediastinal and subcutaneous emphysema. These complications developed during a radical neck dissection and were caused by strong inspiratory efforts of the patient, according to a mechanism suggested by the experiments of Champneys. This mechanism must be distinguished from that of Sante's, Dorwart's, and Escudero and Adams', where the pneumothorax results from the rupture of the overdistended portion of the lung after massive collapse of another portion of the same lung. The patient reported made a satisfactory recovery without other than supportive treatment.

From the literature we have collected eighteen cases of spontaneous pneumothorax that followed operations: Wilks and Moxon, Champneys, Iglauer, Wiethe, Keis, Jehn and Niessen, Gold, Lotheisen, Dorwart, Phillips, Waldron and Vanzant, Weinstein, and Eliason and McLaughlin. Six of these cases had unilateral pneumothorax: Champneys, Iglauer, Dorwart, Wiethe, and Weinstein. Nine cases had bilateral pneumothorax: Wilks and Moxon, Champneys, Keis, Phillips, Waldron and Vanzant, Jehn and Niessen, Gold, and Lotheisen. In three cases the type of pneumothorax was not stated. In six cases the pneumothorax may be considered the cause of death: Wilks and Moxon, Champneys, Keis, Jehn and Niessen, and Gold. Six cases recovered from the pneumothorax: Iglauer, Wiethe, Dorwart, Phillips, Waldron and Vanzant, and Weinstein, while in the remaining six cases neither the cause of death nor the end result was clearly described.

CONCLUSIONS

Spontaneous pneumothorax as a postoperative complication is probably more common than is suspected because it may be overlooked or confused with other postoperative pulmonary or cardiovascular conditions.

Besides the usual signs of pneumothorax, one should look for subcutaneous and mediastinal emphysema.

Pulmonary effort appears to be the principal factor in the production of the complication. This may occur during or after the operation.

The morbidity of the complication is difficult to state because all the cases were not clearly reported, but six out of nineteen patients died as a result of pneumothorax.

After a correct diagnosis has been made, the treatment should be directed toward supportive measures and, if necessary, aspiration of the pneumothorax should be performed.

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Editorials

Dr. Meyer Bodansky

(1896-1941)

DR. MEYER BODANSKY (member of the Editorial Staff of SURGERY), Professor of Pathological Chemistry at the University of Texas School of Medicine, died after a short illness at the John Sealy Hospital, Galveston, Tex., on June 14, 1941. He was born in Russia in 1896 and was brought to America by his parents in 1907. He received his Bachelor of Arts degree from Cornell University in 1918, his Master of Arts degree from the University of Texas in 1922, his Doctor of Philosophy degree from Cornell in 1923, and his Doctor of Medicine degree from the University of Chicago in 1935. During the World War he served in the laboratory division of the Medical Corps. He was instructor and adjunct professor in biological chemistry at the University of Texas from 1919 to 1925. He taught at Leland Stanford University from 1925 to 1926, returning to the University of Texas in 1926, where in 1930 he was made Professor of Pathological Chemistry, a position held until his death, except for one year as visiting professor at the American University at Beirut, Syria, 1922 to 1923. Dr. Bodansky directed the laboratories of the John Sealy Hospital and the John Sealy Research Laboratory.

Dr. Bodansky's research work and writings in physiologic chemistry are widely known and highly respected. His thesis on "The Chemistry of Heart Action" was an outstanding contribution. His textbook *Introduction to Biological Chemistry* is a standard text and is used in medical schools and graduate schools of medicine throughout the world. Other of his widely used books are *Introduction to Physiological Chemistry* and *Laboratory Manual of Physiological Chemistry*. In addition to his many activities, he contributed freely to scientific medical journals, chief of which were SURGERY, *The Journal of Biological Chemistry*, and the *American Journal of Physiology*.

He was a member of the American Society of Biological Chemists, The Society of Experimental Biology and Medicine, the A.A.A.S., American Society of Clinical Pathology, the Texas Academy of Science, and Sigma Chi.

Dr. Bodansky's death was more tragic because it occurred at the height of his productive activity. In addition to being laboratory director, teaching, and doing research work, he was preparing a new edition of his textbooks. With his many achievements he remained

modest and retiring to the extreme. He was kind and sympathetic, and a faithful friend to all his associates and students. He was highly respected by all who knew him and admired by scientists of the medical profession everywhere. His passing is a serious loss to his institution, as well as to medicine and allied sciences.

—*Albert Singleton, M.D.*

Galveston, Tex.

Reduced Temperatures in Surgery

VARIOUS external uses of cold in the form of water, ice, ice bags, and other applications belong to the immemorial traditions of medicine and surgery. New ideas have developed in recent years along two independent lines.

The bold pioneer work of Temple Fay, now gaining more deserved recognition, comprised essentially two innovations: one, radical and prolonged local chilling by means of refrigerating tubes and capsules introduced directly into the tissues; the other, the artificial reduction of general body temperature to levels not previously considered possible in man, maintaining during several days a bodily and mental state which has been compared with the hibernation of lower animals. These methods and the fundamental physical and biological principles upon which they were based became associated in the medical mind almost entirely with the attack upon cancer; but regardless of what may prove to be the ultimate value in this field, Fay has pointed out additional uses ranging from the treatment of infections as serious as brain abscess and gas gangrene to the relief of pain and other neurologic and psychiatric disorders.[1] In Fay's own field of neurosurgery there appear to be fascinating theoretical possibilities that inflammatory reaction may be checked, edema controlled, and the consistency of the nervous tissues made firmer by low temperature so as to facilitate handling and reduce lacerations.

The other line of development, less known and therefore requiring fuller explanation, originated from the problem of diabetic or arteriosclerotic gangrene. States of insufficient circulation were studied through experiments on tissues or organs without any circulation, primarily on animals' legs deprived of blood supply by a tourniquet. It was found that heat markedly accelerated necrosis, while cold permitted the survival of the legs for at least fifty-four hours[2] and of rats' tails for more than ninety-six hours.[3] Shock, thrombosis, and damage to vessels or nerves were also strongly inhibited by cold. These facts, together with the well-known restraint of bacterial activity by reduced temperature, suggested practical applications to treatment.

The guide in these procedures was the familiar preservation of normal or tumor tissues at ice box temperature for weeks or months, apparently without harm. The imitation of these conditions in parts still attached to the body is essentially bound up with the use of a tourniquet, which serves the double purpose of enabling the local part to be chilled thoroughly and accurately and preventing chilling of the rest of the body. After very many experiments in different animal species had demonstrated the retention of both vitality and healing power without any perceptible impairment, the radical proposal still aroused natural misgivings in conservative surgeons. Accordingly it was necessary for Allen to make the first trials on private patients, by taking personal charge and responsibility for the anesthesia. It became possible thus to announce a small series of encouraging experiences.[4] Through Homer Cudmore the method was brought to the attention of Lyman W. Crossman, under whose direction it has since been used on the surgical service at City Hospital, New York City, with participation by W. F. Ruggiero, Vincent Hurley, and other associates, and the helpful cooperation of the heads of other services. The principal experience to date has consisted of amputations for peripheral vascular disease and its complications, but it is expected that reports on other uses will be made subsequently by different staff members.

A series of about forty amputations up to the present cannot be made a basis for too positive claims, especially as the early technique was primitive and greater accuracy and efficiency are expected from the apparatus only now becoming available. Nevertheless it is necessary to state impressions and reasons why the method should be used even experimentally. The following may therefore serve as a summary of the advantages according to preliminary impressions and hopes, subject to any necessary amendments with larger experience: (a) simple and efficient anesthesia, differing from other methods in being an anesthesia of protoplasm as well as of nerves; (b) accordingly, absence of all the usual signs or symptoms of shock; (c) reduced liability to pain, edema, infection, and necrosis, with the aid of postoperative cooling; also freer drainage when necessary; (d) consequently, success sometimes at lower levels of amputation than formerly considered feasible; (e) for all these reasons, lower mortality; (f) slower but healthier healing processes, and better average character of the final scar and stump.

The more limited the circulation, the more completely a limb can be chilled through and through without a tourniquet; therefore theoretically bacterial activity should be arrested more effectively in an arteriosclerotic than in a normal limb, and the local tissue metabolism should be capable of reduction to a level for which the existing blood supply is adequate. This principle seems to succeed in practice to the extent that an advancing arteriosclerotic gangrene can be delayed and

the local color temporarily improved; also a threatening infection can sometimes be checked as regards local symptoms and systemic absorption. Thus far in the experience with peripheral vascular disease these benefits have not extended to the point of a cure by conservative treatment. The patient may be saved in the sense of bringing him into condition to be cured by operation, but as yet the necessity of operation has not been obviated.

The immediate and positive value for the control of pain, shock, and infection strongly recommends this method for traumatic and military surgery. The requisite apparatus for dispensing with the use of ice need not add greatly to the load of a truck or ambulance. Patients with all sorts of limb wounds can thus be transported, or their treatment can be delayed for any emergency reasons, for at least several hours without hemorrhage, pain, shock, growth of gas-forming or other organisms, and also without the harm resulting from a tourniquet at ordinary temperatures. At the end of this time they are ready for operation without an anesthetic and without any added shock. Existing conditions seem to make this one of the most urgent fields for further research.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

SULFANILAMIDE AND ITS DERIVATIVES IN SURGICAL INFECTIONS

A REVIEW

I. THE MODE OF CHEMOTHERAPEUTIC ACTION OF THE SULFONAMIDES*

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MODE OF ACTION

THE earliest observations on the mode of action of the sulfonamides were made largely by clinicians, some of whom conducted laboratory studies supplementing investigations of the therapeutic effectiveness of sulfanilamide in hemolytic streptococcic infections. Leonard Colebrook,[1] who published the first statistically significant clinical report on any of the sulfonamides, one dealing with puerperal sepsis, observed (1936) that "p-aminobenzene sulfonamide (sulfanilamide) has a bacteriostatic and bactericidal action against small numbers of hemolytic streptococci in culture medium and in blood. Following administration of the sulfonamide . . . to man and animals their blood is bactericidal to hemolytic streptococci." It therefore became apparent five years ago that the search, initiated by Paul Ehrlich, for a drug which would be relatively nontoxic for animals and man, and would act upon bacteria in vivo as well as in vitro, had been successful. Study of the peritoneal exudates of infected mice under treatment with sulfanilamide led a number of investigators[2, 3a] into substantial agreement that sulfanilamide brought about a restriction in the capacity of invasive bacteria to multiply within the body and, in addition, probably rendered the surviving bacteria more susceptible to destruction by the phagocytes of the host.

Marshall and his co-workers[4] brought out the fact that sulfanilamide administered to animals and man becomes distributed with remarkable uniformity throughout the body fluids and the tissues bathed by these fluids. It thus appeared probable that the administration of sulfanilamide contributes toward producing a generalized elevation in the bacteriostatic capacity of all of the intra- and extracellular fluids of the body. However, Colebrook himself pointed out that the demonstration

*Part II will appear in a subsequent issue.

of the production by sulfonamides of *bacteriostasis* in vivo was not alone enough to constitute an explanation of the mode of action of the drug in terms capable of being put to practical use in the further development of chemotherapy. It was quite essential to determine precisely how the sulfonamides bring about their interference with the customary growth activity of invasive bacteria. The first step in the development of present concepts of the mode of action of the sulfonamides was through the accumulation of data concerning the factors which tend to increase or diminish the magnitude of the effect of the drug in vitro and in vivo. The present review will show that the evidence so obtained pointed to the fact that the action of the sulfonamides was probably to disturb the operation of an enzyme system upon which the continuation of bacterial multiplication depends. It was then possible for students of the chemistry of bacterial metabolism to approach identification of the particular enzyme system involved.

FACTORS CONDITIONING THE MAGNITUDE OF THE DRUG EFFECT

1. *Ratio Between Concentration of Drug and Number of Bacteria.*—Colebrook[5] noted that "the growth of small inocula of streptococci in culture medium is inhibited by minute quantities of the sulfanilamide, but with large inocula there is no effect, even with a concentrated solution." The importance of the concentration of the drug is obvious and requires little elaboration. Most of the experimental data bearing on this point suggest that the production of bacteriostasis depends upon the existence of a quantitative relationship between the molecular concentration of sulfonamide on the one hand, and the number of bacteria on the other, provided, of course, that the composition of the medium, the temperature, and the age and strain of the culture are controlled. However, the molecular concentration obtainable with any given drug is limited by its solubility; whereas, the number of bacteria and the other factors are subject to wide variation. No agreement has developed among investigators as to the quantitative aspects of the drug-bacteria ratio because, with few exceptions, no two individuals have employed identical conditions for studies in vitro. It is of practical importance to recognize, however, that altering the concentration of the drug induces variations of far less magnitude than altering the composition of the medium or the temperature of incubation. Complete failure of therapeutic response in an infection seems less often to be due to inadequate concentration of drug than to an unfavorable adjustment of other conditions; e.g., a drug-resistant species, or substances in the inflammatory zone which would tend to antagonize the effect of any concentration of drug which might be obtained.[6]

2. *Nutrient Properties of the Medium.*—In 1938 Lockwood[7] called attention to the fact that the inhibitory effect of sulfanilamide on the growth of hemolytic streptococci in human serum was largely removed by the addition to the serum of small amounts of commercial peptone.

Since only the virulent variants of the strains of streptococci which were used showed a capacity to grow in peptone-free human serum, it was suggested that the effect of sulfanilamide might be to prevent operation of an enzyme system necessary to bacteria in splitting or in utilizing the protein substrate. This effect might be of critical importance in a medium such as peptone-free serum, wherein the sources of nitrogen are chiefly in the form of undegraded protein. Once the bacteria ceased multiplying they underwent disintegration and autolysis. The lethal action of the drug upon bacteria was therefore believed to be not a phenomenon of active sterilization, but a subtle interference with an integral nutritive process, leading to death of the cells by "starvation." The addition of peptone offered the bacteria an alternative source of nitrogen, permitting their escape from the bacteriostatic action of the drug. In an effort to account for the failure of concentrated solutions of sulfanilamide to destroy large inocula of streptococci in serum, the author observed that "the death and dissolution of some of the organisms may provide the more resistant survivors with split-products of bacterial proteins which they may utilize instead of serum protein." Although many investigators have confirmed the observation that the bacteriostatic action of sulfanilamide is limited by the presence in the medium of products of the enzymatic degradation of protein,[8, 9] a good deal of doubt has been cast on the validity of the hypothesis which Lockwood advanced, particularly as it related drug action specifically to the protein-splitting activity of bacteria. Fuller, Colebrook, and Maxted[10] were unable by direct methods to detect any effect of sulfanilamide on the weak proteolytic activity of hemolytic streptococci. They also noted that sulfanilamide was active in their peptone-containing medium, and that the addition of serum, which afforded better conditions for streptococcal growth, interfered with the drug effect. Meanwhile, White and Parker[11] published evidence that the bacteriostatic action of sulfanilamide on streptococci was greatly enhanced if the temperature was raised above the optimum for the culture, and that small inocula of streptococci would die out in sulfonamide-containing media at 39°, whether they contained peptone or not. Gay, Clark, Street, and Miles[12] and Weld and Mitchell[13] advanced the view that environmental factors favorable to the bacteria would limit sulfonamide bacteriostasis, and that maximal drug effects are obtainable only in deficient media. According to this concept, peptone interferes with sulfanilamide in a serum medium only by "stimulating" the growth of the streptococci (or other species), and the mutually antagonistic effects of sulfanilamide and peptone are nonspecific, instead of specific, as suggested by Lockwood. However, since other substances which accelerate the growth of streptococci in serum, such as dextrose,[3b] and acid-hydrolyzed peptone[14] fail to antagonize sulfonamide bacteriostasis, and since cultures which have ceased multiplying in sulfanilamide-containing media may be returned to growth activity by the addi-

tion of peptone,[7] there remains the definite probability that commercial peptone, or one of its components, is a specific inhibitor of sulfanilamide action in biologic fluids.

In any event, experimental evidence as indirect as that reviewed up to this point could at most be only suggestive of the nature of the mechanism of the action of the sulfonamides and may not be employed as final proof of any hypothesis. The emphasis upon the nutritional environment of the bacteria in relation to their susceptibility to sulfonamide action had the effect of stimulating further work along similar lines.

Stamp[15] applied himself to a search for other substances in bacteria which would act like peptone in antagonizing sulfanilamide. He obtained from streptococci an extract which did possess this property and was about one hundred times as active as peptone. At about the same time, Fleming[16] was able to show that killed bacteria added to a sulfanilamide-containing culture interfered seriously with the action of the drug. Green[17] obtained an extract from *Brucella abortus* which displayed nonspecific growth-stimulating and sulfonamide-inhibiting properties. Woods[18] made an important advance by tentatively identifying p-aminobenzoic acid as the highly active sulfonamide-inhibiting substance in an extract of yeast. Concentrations of para-aminobenzoic acid of the order of 1:10,000,000 reduced the bacteriostatic effectiveness of 1:10,000 concentrations of sulfanilamide. At the same time Selbie[41] proved that sulfanilamide lost its capacity to protect mice against experimental hemolytic streptococcic infection when p-aminobenzoic acid was administered to the animals along with the drug, thereby establishing, in vivo, the validity of Woods' observations in vitro. Similar confirmation has been reported by McCarty,[19] who finds that para-aminobenzoic acid inhibits the protective action of sulfapyridine on pneumococcic infection in mice. McCarty noted also that p-aminobenzoic acid had no effect on the acute toxicity of sulfapyridine for mice. Similar observations have been reported on human subjects by Strauss and Finland.[20]

The fact that p-aminobenzoic acid is a simple organic compound basically similar to sulfanilamide itself made it possible for Woods to advance an attractive hypothesis of the mode of action of sulfonamides. This hypothesis postulates that p-aminobenzoic acid is an "intermediary metabolite" of essential importance in the process of bacterial cell division. Since p-aminobenzoic acid is not one of the primary growth factors, or substances which must be added to synthetic media in order for bacterial growth to occur, it is assumed that many species of organisms must be able to prepare their own p-aminobenzoic acid from other materials. (Commercial peptone might be a potential source of p-aminobenzoic acid, but attempts to prove this have been unsuccessful.) In order for p-aminobenzoic acid to play its essential role in bacterial metabolism it must be acted upon by a specific enzyme of the cell, and

molecules of sulfanilamide resemble molecules of p-aminobenzoic acid so closely that the two substances compete for position on these enzymes. If all of the positions are gained by molecules of sulfanilamide, which are of no nutritive value to the cell, then the utilization of p-aminobenzoic acid is blocked, and the cell ceases to multiply. Since the affinity of sulfanilamide for position on the enzyme is less than the affinity of p-aminobenzoic acid, complete blockade occurs only when the numerical ratio is strongly weighted in favor of the former; for example, in the case of cultures of hemolytic streptococcus there must be more than a thousand molecules of sulfanilamide for each molecule of p-aminobenzoic acid in order for bacteriostasis to occur. Woods estimates that sulfapyridine is approximately five times as effective as sulfanilamide in competing with p-aminobenzoic acid. Fildes,[21] writing in support of this hypothesis, makes the following statement:

"On this view, the 'sensitivity' of a microbe to sulfanilamide would depend at least in part upon whether it could synthesize p-aminobenzoic acid readily or not. An organism whose synthetic powers were poor would be more sensitive than one with greater power. Similarly, a large number of bacteria would be less affected by a certain concentration of sulfanilamide than a small number. Inhibition or not would become a question of the proportion of sulfanilamide to p-aminobenzoic acid affecting the enzymes of each cell."

Woods'[18] explanation is especially attractive because in addition to accounting for variations in the magnitude of bacteriostasis with changes in the drug-bacteria ratio, it offers a basis for interpreting differences in specificity of the various sulfonamides. It is possible that the attachment of pyridine as a prosthetic group to sulfanilamide raises the affinity of the drug for the "p-aminobenzoic acid enzyme"* in the pneumococcus, and similarly the addition of thiazole increases the specificity for the staphylococcus.

There is no published evidence that the sulfonamide-inhibiting properties of commercial peptone and of tissue digests are due to the fact that they contain p-aminobenzoic acid in some conjugated form. The explanation of the close similarity in properties of these substances awaits further study.

The studies reviewed up to this point have dealt with the effects of sulfanilamide upon bacterial multiplication, and except for the plausible inferences which may be drawn from the work of Woods on p-aminobenzoic acid, there is little which can be used in arriving at a precise chemical definition of the reaction between sulfonamide and bacterium. This review would not be complete without mention of a number of interesting observations which relate sulfonamide action to specific metabolic functions of bacterial cells.

*This term is employed in only a figurative sense, pending the advancement of more direct proof of the existence of such an enzyme.

THE PEROXIDE-CATALASE THEORY OF MELLON.—Mellon,[22] in association with several colleagues, has conducted and published a large number of observations on the action of the sulfonamides as inhibitors of the enzyme catalase. This enzyme is present in abundance in blood cells, exudates, and certain bacteria, and has the property of splitting hydrogen peroxide, liberating molecular oxygen, and therefore preventing the accumulation of peroxide to levels high enough to be toxic to bacteria. Sulfanilamide itself is not strongly antagonistic to catalase, but Mellon believes that certain oxidation products of the drug, including p-hydroxylamino-benzene-sulfonamide, are formed in the body, and he has shown that these substances do tend to inactivate catalase in vitro. According to Mellon's hypothesis, it is the accumulation of peroxide in bacterial cells, brought about by sulfonamide inhibition of catalase, which is responsible for bacteriostasis in vivo. Since hydrogen peroxide is not formed under conditions of strict anaerobiosis, it is a corollary of this theory that the operation of sulfonamide bacteriostasis requires aerobic conditions.

Fox, German, and Janeway[23] and Warren, Street, and Stokinger[24] published experiments which suggested that sulfonamides might poise the Eh of bacterial cultures at a level unfavorable to bacterial multiplication. However, the "poising" effects which they noted were quite possibly the result rather than the cause of bacteriostasis. MacLeod[25] obtained sulfapyridine-susceptible and sulfapyridine-resistant variants of the same strain of pneumococcus, and noted that H_2O_2 accumulated in cultures of the former and not in the latter, thus giving some support to the Mellon hypothesis as it relates to the pneumococcus. MacLeod observed also that the acquisition of sulfapyridine-fastness was associated with a marked loss of dehydrogenase activity for glycerol, lactate, and pyruvate, but not for glucose. Exposure of a sulfapyridine-sensitive strain to the drug caused suppression of the same enzymes.

Fuller and Maxted[26] questioned the validity of the peroxide-catalase theory on the ground that Type 3 strains of hemolytic streptococci, which produce no detectable peroxide in their cultures, are quite susceptible to sulfanilamide. Also, it is difficult to understand how this theory can be reconciled with the known susceptibility to sulfonamides under certain conditions of species as resistant to peroxide as the staphylococcus and the *Bacillus coli*.[27] If there existed some direct evidence (1) that the sulfonamides are active only in oxidized form, (2) that peroxide accumulation on or within bacterial cells actually does occur in spite of the large amount of catalase in body tissues, (3) that bacteriostasis takes place only under aerobic conditions conducive to peroxide accumulation, and (4) that the inhibition of sulfonamide action by p-aminobenzoic acid can be plausibly related to this hypothesis, then it would be possible to accept the peroxide-catalase theory as something more than an interesting and suggestive speculation. In Mellon's most recent paper[28] he has broadened his hypothesis as follows: "In addition to catalase, other enzymes are adversely affected by the

intermediate oxidation products of the sulfonamide compounds. As known so far, they are peroxydase, certain dehydrogenases, and nitratase. The nutrition of the bacteria is thus seriously affected, and bacteriostasis results.''

Effect of Sulfonamides on Cell Respiration.—Neither Barron and Jacobs[29] nor Chu and Hastings[30] were able to show any significant effects by low concentrations of sulfanilamide on the oxygen consumption of the heavy saline suspensions of resting bacteria which they employed in the Warburg apparatus. Kempner, Wise and Schlayer[31] were able to demonstrate marked suppression of the respiratory activity of growing cultures of *Br. melitensis* by 5 mg. per cent concentrations of most of the chemotherapeutically active sulfonamides. These workers showed, however, that the decreased O_2 consumption was a result of bacteriostasis and failed to note any specific action by sulfanilamide on the respiratory enzymes of *Br. melitensis*. West and Coburn[32] studied the effect of sulfapyridine on the synthesis of cozymase by staphylococcus from nicotinic acid in a basal medium deficient in cozymase. Cozymase contains nicotinic acid. When coupled with protein it forms the dehydrogenases—the enzymes concerned with oxidation or energy transfer in cell metabolism. The staphylococcus requires added nicotinic acid in order to synthesize cozymase but grows well if preformed cozymase is provided. When sulfapyridine and nicotinic acid are both added to the medium, growth does not occur, which suggests that the sulfonamide may compete with nicotinic acid for position in the coenzyme molecule. However, if preformed cozymase is present, sulfapyridine has no bacteriostatic effect in this system. Similarly, Dorfman, Rice, Koser, and Saunders[33] have shown that sulfapyridine inhibits the stimulation of respiration of dysentery bacilli by nicotinamide. These observations are of especial interest for two reasons: (1) they offer support to the general hypothesis that the sulfonamides act as competitive inhibitors of certain essential enzyme systems, and (2) they show that a competitive relationship exists between sulfapyridine and a component of the vitamin B complex of related chemical structure, and known to be essential in the metabolism not only of bacteria, but of animals as well. That reactions of this type may account for some of the deleterious effects of sulfonamides on the host is suggested in a recent report of West,[34] indicating that the administration of sulfapyridine will inhibit the curative action of nicotinic acid (but not of coenzymes) on black tongue in dogs. The specific competition between sulfapyridine and nicotinic acid is probably due to the fact that both agents contain the pyridine nucleus. In spite of the suggestive nature of these studies there is as yet no evidence that the administration to patients of nicotinic acid or thiamin will interfere with the therapeutic action of the sulfonamides.

INHIBITION OF TOXIN FORMATION

Since many of the toxins or "agressins" of bacteria are probably enzymic in nature, it would not be surprising if the production or activity of certain toxins might be impeded in the presence of sulfonamide.

Levaditi[2] and Carpenter and Barbour[35, 36] apparently succeeded in inactivating the endotoxin of the gonococcus in vitro with sulfanilamide and reported protection of mice with sulfanilamide against otherwise lethal injections of the toxins of staphylococcus, hemolytic streptococcus, and *Clostridium welchii*. However, neither Bayliss[37] nor Rigdon and Freeman[38] were able to confirm the work of Carpenter and Barbour on staphylococcal toxins. The general opinion of authors who comment on this subject is that sulfonamides do not directly inactivate preformed exotoxins such as streptococcal hemolysin, but tend to limit their production through bacteriostasis.[3c] However, the subject cannot be closed in the face of evidence as suggestive as that of Carpenter and Barbour and of Levaditi, and further work is needed along this line. There would appear to be an open possibility that the sulfonamides may effect unstable combinations with certain toxic bacterial proteins, or endotoxins, and thereby modify their action upon the physiology of the animal.

INFLUENCE OF SULFONAMIDES ON THE PATHOLOGIC SEQUENCE OF ACUTE INFECTION

Regardless of the mechanism of the action of sulfonamides on bacterial metabolism, the end result in vivo appears to be the production of bacteriostatic conditions in the zone of infection, and the protection of uninvolved tissues against bacterial invasion. The evidence for this has been reviewed in considerable detail by Long and Bliss.[3a] That host factors are of great importance in complementing sulfonamide effects in vivo has been demonstrated by numerous investigators, particularly Gay.[39] Bacteria which suffer from restricted reproductivity and toxin production are quite naturally more susceptible to ingestion and destruction by tissue phagocytes than bacteria endowed with full parasitic invasiveness.

An interesting description of the influence of sulfonamide on the course of invasive infection has been presented by W. B. Wood, Jr.,[40] based upon serial observations of changes in the pathologic picture of experimental pneumococcic pneumonia in the rat: "During the first 18 hours the drug had little effect upon the advancing pneumonia. The border of the lesion remained irregular and hemorrhagic, and the many pneumococci in the edema-filled alveoli at the margin indicated that the infection was still spreading rapidly.

"At the end of 18 hours there was evidence that the sulfapyridine was beginning to exert its effect. Examination of the pneumococci in the edema zone showed a striking change in their morphology; many

were swollen, pleomorphic, and irregularly stained, and a few had grown in short chains. Forty-two hours after the start of treatment the edema zone had disappeared completely, the pneumococci at the margin having been overtaken by leukocytes. . . . Organisms could still be seen within phagocytic cells after 66 hours of treatment, but by this time macrophages were numerous in the alveolar exudate and appeared to be taking an active part in destroying the bacteria. On the fourth day no pneumococci could be found in the stained sections, and after one week there was extensive resolution with only macrophages remaining in the rapidly clearing alveoli."

There is evidence that the presence of "inhibitor substances" in the zone of infection will restrict the chemotherapeutic effectiveness of sulfonamides just as it limits bacteriostasis in vitro. The observations of Selbie[41] and McCarty[19] on p-aminobenzoic acid are directly confirmatory of this phenomenon. It has been suggested as a general principle that the resistance to therapy of localized abscesses and necrotizing infections is due in large part to inhibitor substances released by the enzymatic degradation of tissue.[6, 42] MacLeod's[25] discovery of inhibitor substances in a number of organs and exudates, particularly those exposed to enzymic digestion, supplies a sound experimental basis for this supposition. Woods' observation[18] that procaine is an active sulfonamide inhibitor suggests that caution should be employed in administering this anesthetic to patients with active infection who are being treated with sulfonamides.[43] Lockwood[44] has recently prepared a discussion of the application of theoretical considerations regarding the action of sulfonamides to practical problems in surgical therapeusis. It is suggested that the therapeutic result in a given case of established or threatened infection will depend upon the adjustment of three principal variables; namely, the concentration of sulfonamide maintained in the immediate environment of the bacteria, the mobilization of the cellular defense (which of course varies in different tissues), and the concentration of sulfonamide inhibitor substances. In diffuse invasive infections the adjustment of these factors favors effective drug action; in localized or necrotizing infections, sulfonamide therapy will tend to be ineffectual, necessitating surgical intervention. For a particularly interesting discussion along this line the reader is referred to an article by Fleming.[45]

The highly selective action of sulfonamides on bacterial metabolism is evidenced by these two remarkable facts:

1. Concentrations of sulfonamide in the tissues as low as 1 mg. per cent or 1:100,000 will produce demonstrable chemotherapeutic effects.

2. Concentrations up to the saturation level, 200 to 1500 mg. per cent, will produce little, if any, demonstrable local injury to host cells, except perhaps through the action as a foreign body of undissolved

drug. Ehrlich himself could scarcely have foreseen the development of drugs with chemotherapeutic indices as high as these!

Successful chemotherapy in bacterial infections has come about by methods of trial and error, through which we have come to abandon the concept of "therapia sterilisans magna" as the keystone of chemotherapy. We are now provided, instead, with substances which can permeate all of the cells and fluids of the body and render them unsuitable as culture media for many bacterial parasites. Since the sulfonamides are usually not injurious to the host cells, there is no interference with the natural cellular mechanisms of phagocytosis and tissue repair. These are the properties of the sulfonamides which explain and justify their ever-increasing use in surgery.

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Review of Recent Meetings

REPORT OF THE MEETING OF THE AMERICAN ASSOCIATION FOR THE STUDY OF GOITER

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THE annual meeting of the American Association for the Study of Goiter was held in Boston May 12, 13, and 14, 1941. The meeting was opened by **F. E. Rogers,** of Denver, Colo., the President. There were a number of important papers, and frequently during the session the discussions were interesting and prolonged time, showing extreme variability of opinion regarding debatable points.

The first paper was by **J. L. DeCourcy,** of Cincinnati, Ohio, on the importance of maintaining a normal basal metabolic rate following thyroidectomy. He felt that the problem of preventing recurrence of toxic goiter began at the time of the operation. He was inclined to remove too much rather than too little of the thyroid tissue. Almost immediately postoperatively he began giving the patient thyroid extract. This was not only to prevent symptoms of myxedema but also to prevent thyroid hypertrophy, which is more apt to occur if the administration of thyroid extract is omitted. The amount of thyroid extract given was ½ gr. daily for approximately three months. He repeated the basal metabolic rate determination at intervals for several years in order to recheck the possibility of hypertrophy of the gland.

For diffuse nontoxic goiter he advised giving desiccated thyroid in increasing doses. This reduces the size of the thyroid and prevents occurrence of toxic symptoms. He has given thyroid extract to three toxic cases. Improvement followed immediately. He has given as much as 6 gr. of thyroid extract daily to these patients.

In discussing this, **Blair Mosser,** Kane, Pa., said that at the University Hospital in Philadelphia they had given thyroid extract to several patients with goiter. One death resulted which stopped their clinical experiments.

Emil Goetsch, Brooklyn, N. Y., studied cases at the Long Island College Hospital in order to show the relationship of parenchymatous hypertrophy and hyperplasia of the thyroid gland to Riedel's struma. His thesis was that fully developed Riedel's struma began many years earlier as an actual hyperplasia of the thyroid and that the end stage was diffuse fibrosis. He believed that hyperplasia acted as an irritant and produced local inflammatory changes in the thyroid gland that went on to fibrosis. In support of his theory he studied 22 children under the age of 12 years and showed areas of lymphocytic infiltration in the glands removed from these children. In older patients, he found inflammatory fibrosis associated with the areas of hyperplasia. In the areas that did not have any hyperplasia in the glands, there was no evidence of fibrosis.

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John de J. Pemberton, Rochester, Minn., and **Allen Graham,** Cleveland, Ohio, dissented from the idea that true Riedel's struma was the ultimate result of hyperplasia in hyperthyroidism.

J. Lerman, Boston, Mass., gave some further observation of this pituitary type of myxedema. Attention to this type of myxedema was aroused by a patient who apparently had myxedema but who on the administration of thyroid extract went into coma. He cited another patient who on several occasions had had coma following respiratory infection. The patient had some evidence of myxedema, but there were atrophic breasts, amenorrhea, and loss of libido, hypochromic amenia, and a very low basal metabolic rate of minus 40 to minus 52. The cholesterol was low, 112 mg. per cent. The administration of thyroid extract in this case resulted in hypoglycemia. Salt elimination resembled Addison's disease. There was a low blood sodium and chloride. The case was in reality a type of panhypopituitarism. In the treatment the indications were for a high salt diet and gonadogen. The administration of pituitary extract did not prove satisfactory. In myxedema of pituitary origin the blood cholesterol is low or normal. The administration of thyroid extract in these instances may produce an adrenocortical failure.

In the discussion **J. H. Means,** Boston, asserted that the problem was in reality one of "when is myxedema not myxedema?" The answer is: "When it is a kind of 'Simmond's disease.'" He stated that if thyroid extract does not help myxedema, it is probably myxedema of the pituitary type.

D. Henry Poer, of Atlanta, Ga., discussed his experience with the treatment of parathyroid tetany with dihydrotachysterol and vitamin D_2. Dihydrotachysterol was discovered when hyperirradiated viosterol finally resulted in a product in which vitamin factor is destroyed and the calcium-controlling factor highly increased. It was obvious that it was the very thing necessary for the treatment of tetany. Poer had treated 12 cases of tetany. In certain of these the condition was mild and the oral administration of calcium controlled the symptoms (3 cases). Six patients were treated with calcium and dihydrotachysterol. They remained symptom free under this therapy. Two cases were treated with calcium and vitamin D_2. They remained symptom free under this therapy. In the acute cases the administration of calcium and vitamin D and parathormone is indicated, but in chronic cases the symptoms can be controlled with dihydrotachysterol or with calcium and vitamin D_2.

H. B. Friedgood, Boston, discussed experimental exophthalmos and its physiologic and clinical significance. He recalled the work of Shockaert who produced exophthalmos in ducks by repeated injection of anterior pituitary extract and his own subsequent experiments in producing exophthalmos in guinea pigs by the same method. He believes that the exophthalmos factor is different from thyrotropic hormone, because after a period of time the hyperplasia of the thyroid gland resulting from anterior pituitary extract subsides and yet the exophthalmos becomes more pronounced as the injections are continued. Probably the host develops an antibody to the thyrotropic hormone but not to the exophthalmos-producing hormone. The exact cause of the exophthalmos is not explained, but experimentally as well as clinically there is edema of the orbital tissues and muscles.

A. C. Davis, of Rochester, Minn., read a paper on the diagnostic significance of paralysis of the vocal cords in diseases of the thyroid gland. His thesis concerned only cases that had paralysis of one or both vocal cords both before and after operation. In 6,754 cases of adenomatous goiter the incidence of paralysis

before and after operation was 0.4 per cent. In 6,453 cases of exophthalmic goiter the incidence of paralysis was 0.06 per cent. He studied 210 cases of carcinoma of the thyroid of which 163 had sufficient data to include in the report. In 14.7 per cent of these there was a paralysis of the vocal cord both before and after operation. He concluded that finding paralysis of the vocal cord is a distinct aid in the diagnosis of malignancy. However, paralysis is more likely to occur in cases in which the malignancy is a diffused type, when the diagnosis can be made fairly accurately without paralysis. In 57 cases of thyroiditis there was no paralysis of the cord; thus in the instance of a hard gland in which there may be some doubt as to whether the cause is malignancy or inflammation, paralysis of a vocal cord is in favor of malignancy.

In discussing this paper, **Richard Cattell,** Boston, said that the incidence of postoperative paralysis at the Lahey Clinic had been reduced to one-third of its previous 1 to 3 per cent level by routine exposure of the recurrent laryngeal nerve. **John de J. Pemberton** reported a case of bilateral cord paralysis observed preoperatively. Removal of the thyroid gland resulted in restitution of function of the nerves.

R. S. Dinsmore, of Cleveland, Ohio, called attention to the familial factor in exophthalmic goiter in children. He studied 124 cases occurring in children and 14, or 11 per cent, showed a definite familial history. It is true that the larger number of exophthalmic goiter cases develop spontaneously, but the fact that a familial history can be elicited in a large number of cases should indicate the possible etiologic significance of this factor. He reported a child whose mother and grandmother both had exophthalmic goiters.

John Pemberton cited his observation of the occurrence of exophthalmic goiter in identical twins.

Willard Bartlett, Jr., of St. Louis, Mo., reported his studies on the acid-base balance in thyroid disease. In a large number of cases he had studied carbon-dioxide combining power of plasma. These determinations were made on admission, in the preoperative stage, and at the time of discharge on patients who had thyroidectomy for Graves' disease. None of the values were outside the normal range, but more toxic patients have a lower initial carbon-dioxide combining power, and after exertion carbon-dioxide volume per cent falls in the hyperthyroid patient but not in the normal individual. In studying patients on constant diets, he found that the total titrable acidity of the urine excreted in twenty-four hours diminished in the preoperative period of preparation from four to seven times; i.e., as the patient improved. There was evidence of acidosis in hyperthyroidism. The acids are ketone acids and his laboratory has found increases of ketone acids in the blood. He believes that fluids are retained in exophthalmic goiter patients. There is a negative fluid balance.

J. K. McGregor, Hamilton, Ontario, discussed thyroid crisis. He had observed recently 2 cases occurring spontaneously in a preoperative stage. Both the patients had very intense hyperthyroid reactions and 1 died eight hours after admission. The other recovered after remaining in coma for ten days. He wrote to different members of the society and asked their opinions regarding the occurrence of preoperative thyroid crisis. He was surprised to find that it was apparently more common in certain areas than others and that it was not uncommon in New Orleans. He defined thyroid crisis as an overwhelming disturbance of heat-regulating center with intensifications of hyperthyroid symptoms. He outlined a treatment including such measures as intravenous administration of dextrose, oxygen

inhalation, iodine in large amounts, ice packs, rectal irrigations. Thyroid extract has been suggested by some. Preventive treatment is more important than the active treatment since by far the larger number of these cases are postoperative. The stage operations are indicated for certain patients. There was a long discussion concerning this subject. The paper was discussed by **A. L. Lockwood,** Toronto, **Willard Bartlet, Jr.,** St. Louis, **G. C. Shivers,** Colorado Springs, Colo., **Martin Tinker,** Ithaca, N. Y., and **Howard Mahorner,** New Orleans. **Willard Bartlett, Jr.,** indicated that the febrile reaction was not the only aberrant part of this picture. Even if one was able to reduce the temperature to normal by cold baths, patients may go ahead and die irrespective of that. The discussion in general indicated the absence of anything specific with which to combat these cases and the difficulty of handling crisis once it has begun.

D. M. Clute, of Boston, Mass., read a paper on the clinical relationship between iodine feeding and the operability of goiter. In 750 goiter patients 283 had exophthalmic goiter. Forty-seven per cent of these had had iodine before coming for surgery and 53 per cent had had no iodine. He was able to perform one-stage thyroidectomy on only 60 per cent of the patients who had had iodine and on 87 per cent of the patients who had not had iodine before coming for surgery. He indicated that operation was safer after the first administration of iodine and that the administration of iodine promiscuously in the medical treatment of goiter was no favor to the patient.

The second morning of the meeting was taken up with clinical demonstration at the various hospitals in the city. These observers visited the surgeons at the Lahey Clinic, at the New England Deaconess and the New England Baptist Hospitals, seeing there a number of thyroidectomies performed by **Frank Lahey, Richard Cattell,** and **Herbert Adams.** These surgeons demonstrated exposure of the recurrent laryngeal nerve which they accomplished with facility and without loss of time. A case of Hashimoto's disease was presented by **Richard Cattell.**

F. E. Rogers read the presidential address. He reviewed the development and treatment of goiter. In ancient times the Chinese chewed seaweed as a treatment for goiter. The first monograph on goiter was published in 1556 by Thomas Wharton. In 1791 Desault performed a successful thyroidectomy. Coindet, of Geneva, first used iodine for goiter in 1820. Billroth in 1877 reported the injection of iodine directly into the gland. Billroth stated that 29 out of 35 cases were cured by this method. At this time, Billroth had performed thyroidectomy 20 times for goiter. Eight of these patients died of sepsis. In 1880 Sandstrom discovered the parathyroid glands, but their function was not defined until 1891 by Gley. Murray, of England, first used thyroid extract to cure myxedema in 1891. In 1893 Fredrick Mueller discovered increased metabolism or gaseous exchange in hyperthyroidism. The active use of the basal metabolism for diagnosis for thyroidism, however, did not come into general use until about 1917. In 1914 Kendall isolated thyroxin and in 1922 Plumber reported the use of iodine preoperatively and more or less standardized our modern preoperative preparation for thyroidectomy. Numerous other interesting advances were brought out in Roger's paper including some of the more modern ideas of the management of goiter.

V. E. Chesky, Halsted, Kan., discussed the incidence of liver damage in thyroid disease. In 300 consecutive goiter cases at the Hertzler Clinic liver function tests have been done. The hippuric acid test was used and in nontoxic nodular goiter 100 per cent of the cases had a normal liver function; whereas, in the toxic nodular goiter only 67 per cent had normal liver function and 12 per cent had severe liver damage. In diffuse colloid goiter 72 per cent had normal liver

function and 9 per cent had severe liver damage, and in hyperplastic goiter only 43 per cent had normal liver function and in 41 per cent the liver damage was found to be severe. He felt that it was possible to increase liver function preoperatively. Some of the measures used for the improvement of liver function for the administration of liver concentrate, vitamin B complex, glycine (6 Gm. a day), and dextrose.

A paper by **S. Hertz, R. Williams,** and **J. H. Means,** of Boston, on Graves' disease with dissociation of oculopathy and thyrotoxicosis, was read by **R. Williams.** In twenty years at the Massachusetts General Hospital they found the records of 89 patients with marked exophthalmos, papilledema, lid retraction, and failure of extraocular movements. In the group of patients they discussed the basal metabolic rate was usually low. Thirty-nine of the patients had not been operated upon. They felt that the result as far as the eye was concerned was worse in the operated group. Their explanation was that the thyroid activity antagonizes the pituitary output of thyrotropic hormone which they believed is a factor in exophthalmos. They think removal of the thyroid gland results in further increase in the output of thyrotropic hormone. They experimented on rats. Thyroidectomy increased the body water from 66 to 70 per cent and the administration of thyrotropic hormone made still further changes in body fluids. They recommended the administration of thyroid extract and the avoidance of operation in such cases if possible.

This paper was discussed by a number of thyroid surgeons of large experience. In general they did not agree that operation should be withheld in these cases. **A. L. Lockwood,** Toronto, said he believed the best treatment for an exophthalmos due to exophthalmic goiter was early thyroidectomy and that it did not seem advisable to withhold the benefit of thyroidectomy from patients with hyperthyroidism for fear the exophthalmos would get worse.

On Tuesday evening the Association held its annual dinner. **E. H. Rogers** served as toastmaster. **T. C. Davison,** Atlanta, Ga., presented a Memorial Gavel to the Association, a gavel made from wood taken from a dogwood tree on the farm of Crawford Long.

Frank Lahey traced the development of thyroid surgery from an unpretentious beginning to its present extensive importance. Reduction in mortality was ascribed to developments in operative technique, handling of complications, and anesthesia. In reviewing over 20,000 cases, Lahey discussed in turn apathetic hyperthyroidism, multiple-stage operations, thyrocardiac cases, and the relation of function of the liver to thyroid disease. He showed a moving picture illustrating the technique of removal of an intrathoracic goiter too large for intact delivery.

The Van Meter Prize was awarded to **Asher Chapman,** of the Mayo Clinic, for his studies on **Relationships of the Thyroid and Pituitary Glands to Iodine Metabolism,** and **Extra-Thyroidal Iodine Metabolism.**

The first honorable mention was given to **L. A. Turley,** Ph.D., and **E. M. Richter,** Ph.D., of the University of Oklahoma, for their work on **Relation of Lymphocytosis to Hyperthyroid States.**

The second honorable mention was awarded to **Wm. L. MacKenzie King,** of the Mayo Clinic, for his research on **So-Called Lateral Aberrant Thyroid Tumors.**

Asher Chapman discussed **Relationships of the Thyroid and Pituitary Glands to Iodine Metabolism.** He studied three sets of animals: intact, thyroidectomized, and hypophysectomized. These were further divided into subgroups, on normal and subnormal iodine intake. An increase in the thyrotropic hormone was found in the urine of thyroidectomized animals. Studies were made of the response (weight, acinar appearance, and vascularity) of the thyroids of intact animals to the stimulus of low iodine intake. A similar study was made on the hypophysectomized animals, and it was found that the thyroid gland is able to respond to the stimulus of low iodine intake in the absence of the pituitary gland. The response of hypophysectomized animals is similar in kind and proportion to that in intact animals, though starting from a different level.

T. O. Young, Duluth, Minn., in **Surgical Treatment of Thyrotoxicosis as Related to Geriatrics,** cited statistics showing that (in Duluth) although there is a decrease in thyroidectomies in general, there is an increase in the aged undergoing thyroid surgery and also in the aged receiving medical care for thyrotoxicosis. Apathetic hyperthyroidism is relatively more frequent in the aged. The importance of preoperative preparation and of multiple-stage operations on the aged was stressed. The use of vitamin B (especially B_1) and of oxygen and moderation in sedation were advocated.

Irvin Abell, Louisville, Ky., Chairman of the Defense Committee of the American Medical Association, was called upon for a few remarks. He discussed the committee's work and recent developments as regards deferring (from draft) medical students and interns, pointing out that the production of doctors must not be bottlenecked.

J. H. Hutton, Chicago, Ill., discussed nonthyroid conditions causing low and high basal metabolic rates. He reported cases of patients with obesity taking thyroid extract without increase in pulse rate and with loss of weight. He also discussed Fröhlich's syndrome and thin patients with low basal rates. Patients with low basal rates without thyroid symptoms are probably not hypothyroid, especially if they do not become better on thyroid medication. One must consider pituitary and adrenal deficiencies in this respect.

J. W. Hendrick, Amarillo, Tex., in **Use and Abuse of Iodine in the Management of Goiter,** reviewed 600 cases, of which 512 had received iodine treatment; the remaining cases had not had iodine therapy and had not been previously diagnosed. Hendrick suggested the use of iodine during pregnancies in endemic regions and in treating nontoxic goiters especially in school children. Results obtained from a questionnaire sent out to members of the Association were given. This dealt with the use of iodine. In mild hyperthyroidism 88 per cent of those answering prefer operation after lugolization. In mild recurrent cases 70 per cent try control with iodine; in treating nontoxic nodular goiter 99 per cent are opposed to the use of iodine. In preparing toxic nodular goiters 79 per cent are in favor of using iodine.

J. de J. Pemberton, Rochester, Minn., read a paper on **Papillary Adenocarcinoma of the Thyroid.** There are two schools of thought as to origin: (1) stimulation of inferior thyroid tissue rests; (2) metastases secondary to carcinoma of the thyroid. Those patients in whom lateral cervical tumor was the main complaint were classed as having aberrant thyroid tissue irrespective of the thyroid gland. The second group comprised cases in which malignancy of the

thyroid gland was the main complaint and in these the lateral masses were considered as metastatic. In all cases of both groups all the lateral nodes should be completely removed together with the entire thyroid lobe on that side whether or not a tumor is felt in the lateral lobe. Postoperative irradiation should follow. If the carcinoma is of the papillary type, the prognosis is not bad.

J. B. Kent, Denver, discussed **One Reason for Failure in the Surgical Control of the Toxic Hyperplastic (Exophthalmic) Goiter.** According to his view postoperative crisis is in proportion to the amount of gland left and is due to the secretion of this gland residue and does not occur after total thyroidectomy. For these reasons he is opposed to multiple-stage operations.

E. J. Bartels, Boston, found in studying diarrhea in hyperthyroidism that 92 per cent of cases with hyperthyroidism have exaggerated peristalsis. Possible causes of diarrhea in hyperthyroidism were listed: direct action on musculature, vagal action, reduction of gastric acids, retarded absorption, altered pancreatic secretion, reduced hepatic function, altered adrenal function. Lipocaiac is a specific internal secretion of the alpha cells in the pancreas and is distinct from insulin. It has to do with handling of fat. It is active when given either hypodermically or by mouth. Hyperthyroidism has a depleting effect on the alpha cells of the pancreas. Six cases of hyperthyroidism with diarrhea were treated with lipocaiac with restitution of bowel function to normal. The treatment is considered as supplementing the secretion of the alpha cells of the pancreas.

W. O. Thompson, Chicago, discussed **Persistence and Recurrence of Toxic Goiter Following Subtotal Thyroidectomy.** There are remissions and relapses in cases of recurrent and persistent hyperthyroidism just as in cases of hyperthyroidism before operation, and the size of the tissue likewise changes. If iodine will not hold the recurrent or persistent case within reasonable limits, a second operation should be performed. Psychic trauma and its effects were discussed. Cases operated upon by more experienced surgeons have less postoperative thyrotoxicosis. Sometimes the amount of tissue left seems to have little to do with the problem.

In the discussion, **Allen Graham,** Cleveland, and **V. E. Chesky,** Halsted, Kan., considered the behavior of the remaining lobe after lobectomy in hyperthyroidism.

Martin B. Tinker, Ithaca, N. Y., gave a most interesting survey of the history and development of thyroid surgery with which he has been intimately connected. Thyroidectomy for uncomplicated goiter has a negligible death rate, but the multiple-stage operation for hazardous cases is still not used as often as necessary. The advantages of the electric knife were discussed. Tinker advocated wider use of multiple-stage operations. Packing and temporary closure are especially called for in cases of suppurative thyroiditis and extensive malignancy. In cases of extensive malignancy he advocates excision with the electric knife of what can be removed and radiation of the rest.

C. N. Carraway, Birmingham, Ala., and **T. C. Davison,** Atlanta, Ga., reported **The Use of Sodium-Pentothal-Oxygen Anesthesia in Thyroid Surgery.** The chemistry of sodium pentothal was discussed and its action on the central nervous system. The medulla is last affected. Rapid action is obtained via the blood stream. Oxygen administration obviated anoxemia. Atropine given preoperatively prevents secretion and laryngeal spasm. Picrotoxin is an antidote

(0.3 per cent). Studies were given of blood chemistry and liver function before and after the use of sodium pentothal. Electrocardiographic studies during pentothal anesthesia were presented and moving pictures were shown. The conclusions drawn are that sodium pentothal produces a condition most resembling sleep. Oxygen must be given during anesthesia. A large series of cases was reported.

J. H. Vanden Berg, Grand Rapids, Mich., read a paper on **Mild Unrecognized Hypofunction of the Thyroid.** Cases of mild hypothyroidism with so-called normal basal metabolic rates were discussed. These patients have too little physical reserve; they lack "pep" and have little vitality. Mild and unrecognized hypothyroidism is very definite and more distressing than mild unrecognized hyperthyroidism. Too many of us accept the range of minus 10 per cent to plus 10 per cent of the basal metabolic rate as normal. Under thyroid medication the rate may not be raised although the patient improves.

MEETING OF THE AMERICAN SURGICAL ASSOCIATION, APRIL 28-30, 1941, WHITE SULPHUR SPRINGS, W. VA.

J. Dewey Bisgard, M.D., Omaha, Neb.

ADDRESS of the President, David Cheever, Boston.—A scholarly historical review of the influence that wars have had upon the development of the art and science of surgery and of surgeons and the influence that this art and science has had upon the outcome of wars and the fate of civilization, this address, as a classic in content and composition, cannot be reduced to an abstract and must be read in its entirety.

Intestinal Antisepsis, With Special Reference to Sulfanilylguanidine, Warfield M. Firor and (by invitation) **Edgar J. Poth,** Baltimore.—Experiences with this drug in both clinical cases and experimental animals have confirmed previous observations that it is not absorbed as rapidly from the bowel as the other sulfonamides and is more effective in reducing the concentration of coliform organisms in the intestine. The reductions in bacterial flora following its use have not been sufficiently consistent or significant, however, to warrant its use as preoperative measure for intestinal surgery. Some cases, particularly those with ulcerating lesions of the bowel, are entirely refractory to the drug and others show reductions in bacterial counts only after the administration of enormous doses. No severe toxic symptoms have been observed. The use of the drug is contraindicated in the presence of obstruction, ulcerating lesions, and renal damage.

Harvey Stone, Baltimore, reported that he had used the drug in 8 cases of ulcerative colitis with no apparent benefit and observed also in 25 cases preparatory to colonic surgery without significant bacteriologic or clinical benefit to warrant continuing its use in the future.

Aseptic Immediate Anastomosis Following Resection of Carcinoma of the Colon, John H. Gibbon, Jr. and (by invitation) **Clare C. Hodge,** Philadelphia.—A comparative analysis of the mortality in 118 cases of resection of the abdominal colon by the techniques of closed exteriorization, open primary anastomosis, and aseptic primary anastomosis was given. This is a collected series from several surgeons.

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The mortality with aseptic anastomosis (Kerr technique) was 13 per cent, that with the other 2 techniques, 28 per cent. Resection should not be done in the presence of obstruction. The obstruction should be relieved by cecostomy before resection is undertaken.

Wm. B. Parsons, New York City, emphasized the importance of the Miller-Abbott for both pre- and postoperative decompression in these cases, often eliminating the necessity of cecostomy. The use of the tube in his series of cases had resulted in a reduction of mortality from 22 to 6.7 per cent. **Harry B. Kerr,** Washington, D. C., reported 107 resections with a mortality of 15 per cent in 39 performed by the aseptic technique as contrasted to 35 per cent in 68 performed by the other techniques. **Richard B. Cattell,** Boston, reported 275 resections carried out at the Lahey Clinic by the closed exteriorization technique with a mortality of 13 per cent. **Leo Eloesser,** San Francisco, described a method of anastomosis by telescoping or invaginating the end of one loop into the other. He believes this gives greater assurance against leakage.

Surgical Management of Carcinoma of the Ampulla of Vater and Distal End of the Common Duct, Verne C. Hunt, Los Angeles.—Ampullary and periampullary carcinomas are usually of relatively low grade malignancy and often are resectable. Diagnosis is suggested by persistence of occult blood in the stool in presence of painless jaundice.

Four (personal) operated cases were reported, 2 of transduodenal resection with reimplantation of the ducts and 2 of the one-stage Whipple operation; 3 survived with good operative results. Operation has been made much safer by control of the hemorrhagic tendency of these jaundice cases with vitamin K. Pancreatic fistula has been a dangerous, troublesome, and rather constant complication of the Whipple operation. It did not occur in Hunt's last case in which the technique was modified by cupping the resected end of the pancreas with the open end of duodenum left after resection of its proximal portion.

Allen O. Whipple, New York City, discussed the advantages of the one-stage operation and reported 1 case successfully resected in one stage. **Thomas Orr,** Kansas City, Mo., reported 2 cases successfully resected by the Whipple technique, one in two stages and one in one stage. Both had pancreatic fistulas which closed; both are well. **Dallas B. Phemister,** Chicago, reported 3 cases and demonstrated that it is possible in some cases to demonstrate the presence of a tumor by special and careful x-ray studies. **Morris K. Smith,** New York City, emphasized the difficulty in palpating the tumor at operation and reported 1 case in which gall bladder drainage was established at the first operation and tumor found upon reoperation for persistence of obstruction.

Results of Partial Gastrectomy for Bleeding Duodenal, Gastric and Gastrojejunal Ulcers, Waltman Walters and (by invitation) **William H. Cleveland,** Rochester, Minn.—Of 122 patients on whom partial gastrectomy was performed at the Mayo Clinic for bleeding duodenal, gastric, or gastrojejunal ulcers, the follow-up study disclosed that partial gastrectomy for bleeding ulcers of the stomach and duodenum was followed by excellent results in from 90 to 94 per cent of cases; hemorrhages and symptoms of ulcer did not recur. This was true, however, in only 80 per cent of cases in which operation was performed for bleeding gastrojejunal ulcer. Of 100 patients traced, only 1 died after gastrectomy from hemorrhage. In the group of cases in which hemorrhage occurred after gastrectomy, there was usually but a single episode which was not serious. Occasionally the hemorrhage was associated with an ulcer type of pain. Most of the cases in which

the symptoms persisted were those in which the pylorus had not been removed or in which enteroanastomosis had been performed at the time of partial gastrectomy. The operative mortality during active hemorrhage is no more than 5 per cent if done early but is very high (30 to 100 per cent) if done late when the patient is exsanguinated.

J. V. Bohrer, New York City, presented statistics showing that although hemorrhages are more often fatal in patients over 45 years of age, they not infrequently cause death in the younger individuals. **M. M. Zinninger,** Cincinnati, reported a series of 92 cases with bleeding ulcers in which 10 per cent died of hemorrhage.

Gastric Ulcer: The Significance of This Diagnosis and Its Relationship to Cancer, Arthur W. Allen and (by invitation) **Claude E. Welch,** Boston.—A study has been made of all cases diagnosed as gastric ulcer admitted to the Massachusetts General Hospital during the period 1930-1939. It is shown that cancer of the stomach was present, rather than ulcer, in 12 per cent of all the cases, and in nearly 40 per cent of those cases in which resections were performed and pathologic sections were available. The present method of treatment of gastric ulcer, implying medical observation for a period of time, results in a considerable delay in the diagnosis of many gastric cancers and overlooks a definite hazard of medical therapy. Subtotal gastrectomy can now be performed for gastric ulcer with a reasonable mortality (6.4 per cent in the past five years). This produces almost uniformly excellent results if the lesion is found to be a benign ulcer, a comparatively high percentage of cures if cancer is present. It is therefore proposed that gastric ulcer be considered fundamentally a disease demanding surgical therapy and that a short period of medical treatment be condoned only if the ulceration is acute, inaccessible, or in a poor-risk patient. Gastroscopic examinations in these cases did not prove to be more accurate than x-ray studies in differentiating ulcer and carcinoma.

Frank Lahey, Boston, pointed out that at the Lahey Clinic only 7 per cent of duodenal ulcers are treated surgically; whereas, 27 per cent of gastric ulcers are operated upon. **J. S. Horsley,** Richmond, Va., stated that partial gastric resection is indicated in most cases of gastric ulcer. **Fordyce B. St. John,** New York City, stated that most statistical reports of permanent cures of ulcers are relatively premature because ulcers do recur after a quiescent period of as long as ten years or more. **R. Graham,** Toronto, reported a diagnostic error of 9 per cent in question of ulcer and carcinoma of the stomach in his series of cases. He also reported an operative mortality of 35 per cent in cases operated upon during a massive hemorrhage.

Skin Grafting and the "Three-Quarter-Thickness" Skin Graft for Prevention and Correction of Cicatricial Formation, Earl C. Padgett, Kansas City, Mo.—The technique of using the author's dermatone and the advantages offered by it were well demonstrated. With it a large sheet of skin of any desired thickness and of constant thickness can be cut rapidly not only from the thighs and abdomen but from such surfaces as the thoracic wall. The three-quarter-inch-thickness graft is the most ideal for most purposes. It is thick enough to give an excellent cosmetic and functional result and contains sufficient derma to minimize contractures. It is more likely to survive transplantation than a full-thickness graft. He reported a survival record of 96 per cent.

Robert H. Ivy, Philadelphia, warned of the need of experience in the use of the dermatone. **V. Blair,** St. Louis, stated that grafts cut with the dermatone

take better because the cut surface is smooth and even and in the cutting the skin suffers less trauma.

Total Thoracic and Partial to Total Lumbar Sympathectomy and Celiac Ganglionectomy in the Treatment of Hypertension, Keith S. Grimson by invitation of **Dallas B. Phemister**, Chicago.—There are two types of experimental essential hypertension, a neurogenic type and a type produced by renal ischemia. Experimental studies related to the role of the sympathetic nervous system in part and as a whole in blood pressure regulation and in experimental neurogenic hypertension have suggested that more might be accomplished by total paravertebral sympathectomy than by splanchnic section alone. Complete removal by a two-stage transpleural operation of the thoracic and lumbar paravertebral sympathetic chains, the splanchnic nerves, and the celiac and first lumbar ganglia has been performed on 8 patients with essential hypertension. In 2 other cases the operation consisted in complete bilateral thoracic sympathectomy, removal of the splanchnic nerves, and celiac and first lumbar ganglionectomy. Lowering of the blood pressure has been observed in all instances varying from complete restoration of the blood pressure to normal to only moderate lowering.

R. H. Smithwick, Boston, stated that he had approached the problem by carrying out resection in stages until the desired result had been obtained. In 9.1 per cent of cases a good result was obtained by the Peet operation and in these cases no further resection was done. In the remaining cases the lumbar ganglia and trunks and celiac ganglia were resected with good results in 65 per cent. In the cases in which these two procedures failed to give the desired result the upper dorsal ganglia were resected. **George Curtis**, Columbus, Ohio, stated that splanchnic section for hypertension has demonstrated the presence of sensory fibers in the splanchnic nerves. The motor influence of splanchnic section upon the motor activity of the stomach was demonstrated in tracings of peristalsis. **Loyal Davis**, Chicago, stated that sulfocyanate was more effective in reducing blood pressure after sympatheticosplanchnic section even in cases in which the operation fails to lower the blood pressure significantly. **M. M. Peet**, Ann Arbor, Mich., noted that a review of 700 operated cases has shown not only symptomatic improvement in most cases but a definite prolongation of life as judged by the Wagner-Keith mortality table.

Intracranial Aneurysms: Diagnosis and Surgical Treatment, Walter E. Dandy, Baltimore.—One-half of the intracranial aneurysms arise from the circle of Willis and are not accessible or amenable to operative treatment. Congenital aneurysms of the intracranial carotid which can be treated surgically are of two types: (a) those in the canal are treated by ligating the artery in the neck and then clipping the neck of the aneurysmal sac or the artery itself within the cranium; (b) those of the intracranial trunk are exposed and either the neck of the sac is ligated or the sac trapped between ligatures. Reported were 13 operated cases of which 10 were cured. The symptoms are third nerve palsy and pain in the eye of the affected side.

Francis C. Grant, Philadelphia, pointed out that thorotrast is useful in locating and identifying these aneurysms in suspected but doubtful cases.

Observations on Intrathoracic Neoplasms, John Alexander, Ann Arbor, Mich.—Accurate preoperative diagnosis of intrathoracic neoplasms, apart from esophageal carcinomas and those bronchogenic carcinomas that can be biopsied endoscopically, is virtually impossible. In many instances the surgeon cannot tell before operation if a tumor is benign or malignant and if it should be malignant, whether or not

it is removable. As certain benign tumors are potentially malignant and as many malignant tumors may be removed completely, practically every case of intrathoracic tumor should be promptly explored surgically if there is no evidence of metastasis or hopeless invasion of the adjacent thoracic walls. Preoperative pneumothorax is rarely informative except in distinguishing between pulmonary and mediastinal or thoracic wall tumors. Tumors that might be lymphoblastomatous should be given a diagnostic test dose of deep x-ray therapy. The difficulty of differentiation between the expansile pulsation of a mediastinal aneurysm and the transmitted pulsation of a true neoplasm was emphasized.

S. W. Harrington, Rochester, Minn., emphasized the importance of lateral and oblique roentgenograms in diagnosis. Two cases of substernal diaphragmatic herniation were reported showing difficulty in their diagnostic recognition.

Endometriosis: Its Significance, Joe V. Meigs, Boston.—In 363 consecutive abdominal gynecologic operations, gross or microscopic evidence of endometriosis was found in 25 per cent of cases. It is much more commonly encountered in private patients than in those of charity clinics. Late marriages and late conception may be etiologic factors.

James C. Masson, Rochester, Minn., stated that he had not observed any evidence of social sexual relationship to the occurrence of endometriosis.

Symposium of Surgical Preparedness: Emergency Treatment of War Injuries of the Face and Jaws, Robert H. Ivy, Philadelphia.—A correlated plan of treatment from the advanced zone to the installations in the rear shortens the average period of disability of this type of injury and increases the number ultimately restored to approximately normal function and appearance. Control of hemorrhage and treatment of shock are the most urgent early considerations. Establishment of adequate air passage demands special measures. In fractures of the jaws, any bone fragments still attached to soft tissues should be carefully preserved. Carelessness in early cleansing of wounds and removal of shattered fragments frequently results in loss of important segments, malunion, nonunion, and secondary deformity. Temporary fixation of bone fragments should precede closure of soft tissues where possible. In fixation of jaw fractures collaboration of surgeon and dental officer is essential. In transportation from the combat zone, cases of oral and pharyngeal wounds preferably should sit up. If he must be recumbent, the patient should be placed face down if there is danger of obstruction in the air passages.

Lieut. Col. Roy A. Stout, Dental Corps, U. S. Army.—Fractures of the jaw are treated by wiring of teeth when available, otherwise by traction applied through a fixed point in front of the face or by internal fixation. A fixed point for applying traction can be established with a tongue depressor fixed to the forehead and along the bridge of the nose or a wire tripod in front of the face fixed to a plaster headgear. **V. Blair,** St. Louis, stated that bad cosmetic results are usually attributable to poor initial treatment rather than to actual destruction. **James B. Brown,** St. Louis.—Often fragments can be fixed with Kirschner wires. Loose fragments should always be preserved and used in restoration.

Organization for Evacuation and Treatment of War Casualties, N. T. Kirk, Colonel, M. C., U. S. Army (by invitation).—The general plan of organization for the emergency treatment and evacuation of the injured from front lines to the base hospitals was presented.

The Cooperation Between the Army Services of Evacuation and Hospitalization, Henry H. M. Lyle, New York City.—Active intelligent cooperation predicates a basic knowledge of the objects desired, the mechanism by which they are to be accomplished, and the character of the personnel. The speed of attack, and the greater use of automatic weapons, has increased the difficulties of the medical department. The technique of triage, surgical management, and evacuation will have to be adapted to the tactics of mechanization and movement, but the principles remain unchanged. In the last war, military operations assumed the traditional fan-shaped pattern; today it is a war of depth. An open slashing attack has to be met with an equally mobile defense. Aeroplane transportation of the wounded has possibilities, but motor transportation remains the mainstay. The basic principle of military surgery is débridement; chemotherapy is an adjunct. Immobilization in plaster should be of value in transporting the wounded. The consultants should be more active with the service of evacuation and hospitalization.

The Role of the Medical Department in Naval Warfare, F. R. Hook, Commander, M. C., U. S. Navy (by invitation).—The nature of the navy imposes greater individual responsibility upon members of its medical corps. A medical officer may have sole responsibility for the ship's complement. Burns and drowning are frequently encountered in addition to the ordinary injuries. He stated the navy wishes to have available a large medical reserve corps for research and teaching and emergency needs.

Wm. Darrach, New York City, pointed out that in war the lightly wounded are of first importance and should receive preference in care and evacuation. **Elliott Cutler,** Boston, stated that no country in the world has available such a wealth of medical and surgical talent. "Give us the tools and necessary equipment and we will furnish the personnel." During the last war there were distressing gross deficiencies in such essential equipment as laundries.

Leonard R. Broster, M.A., M.D., M.Ch. (Oxford), F.R.C.S. (England) (by invitation), London, England.—Experience in Spain and in the war to date has established the Winnet-Orr method of treatment of wounds as the method of choice for war injuries. It has given uniformly better results in respect to both mortality and morbidity. The wounds are left open and insufflated with sulfanilamide powder. The sulfonamides are administered by mouth. The local treatment of burns has consisted of washing the involved areas with salt solution, drying them, and then applying sulfanilamide powder and an escar with tannic acid or covering the areas with glycerin especially about the face. As a result of bombing two new types of injuries are frequently observed, the blast injuries and the crush syndrome. The former is characterized by hemorrhage from the lungs which present torn alveoli and grooved impression of the ribs on the surfaces. The latter is characterized by severe shock and by hemorrhages into various organs, particularly the adrenals.

The Experience of the Canadian Army With Amputations of the Lower Extremity, W. E. Gallie, Toronto.—Through the Department of Pensions and National Health it has been possible to keep an accurate record and to make frequent examinations of all Canadian Veterans of the last war who have amputation stumps. These observations have shown that for working men end-bearing stumps, the Syme and Gritti-Stokes, are infinitely more useful than other types. Amputations between the ankle and knee should leave a stump not longer than six inches and the fibula should be cut shorter than the tibia. Flaps that are too long and loose and neuromas have been the most frequent causes of trouble.

N. T. Kirk, M. C. U. S. Army, expressed a more favorable opinion of the "below-the-knee" amputations. **L. Eloesser,** San Francisco, stated that with proper construction of the artificial limb "below-the-knee" stumps could be made partially end-bearing and very satisfactory.

B.I.P.P. and Liquid Paraffin Treatment of War and Civilian Wounds, Fraser B. Gurd and (by invitation) **L. H. McKim,** Montreal.—In 1915 Rutherford Morison introduced B.I.P.P. packs for dressing wounds. This paste containing bismuth and iodoform in liquid petrolatum is applied to either fresh or infected granulating wounds. In fresh wounds it is applied to the surfaces after the wound has been débrided and the surfaces dehydrated with alcohol. The wounds are left open, dressed infrequently, and immobilized. The surfaces rapidly become covered with clean healthy granulations permitting early secondary closure. Histologic studies of granulations showed minimal edema and very few leucocytes. Bismuth and iodoform poisoning can be prevented by the judicious use of B.I.P.P. A warning of impending bismuth poisoning is manifested by a "lead line" of the gums.

Present-Day Treatment of Compound Fractures, Robert H. Kennedy, New York City.—The problems in the treatment of compound fractures were discussed generally. Shock and hemorrhage are the urgent and first problems to be met, then the wounds should be cleaned and débrided and the fractures reduced. Kennedy believes the wounds should be left open to close by granulations or by secondary suture. Reduction in most of his cases is accomplished and maintained by traction. The sulfonamides have been administered routinely as has tetanus and gas antitoxin. There is an increasing need for more training of medical students and young surgeons in the accepted methods of treating fractures.

Kellogg Speed, Chicago, stressed the need of more undergraduate and postgraduate instruction in the care of wounds and fractures. During the present war the civilian casualties have exceeded those of combat. Both for the purposes of instruction and military use the types of splints and other armamentarium should be standardized. **Wm. Darrach,** New York City, believes that the fractures should be reduced at the time the wounds are cleansed. **J. A. Key,** St. Louis, believes that it is safe and desirable to do a primary closure of most compounded wounds if cleansed, débrided, and sulfonamized within a few hours after injury. **J. Dewey Bisgard,** Omaha, Neb., presented experimental evidence that the much used chemical bacteriocidal agents usually fail to destroy all bacteria in wounds and seriously injure tissue cells thereby crippling the normal local defense against the bacteria which remain viable in the wounds. Débridement and copious saline irrigations rid the wound of most microorganisms and leave the tissues uninjured to cope with those that remain in the wound. Sulfanilamide causes little or no injury to tissues.

The Treatment of Compound Fractures Resulting From Enemy Action, Philip D. Wilson (by invitation), New York City.—The Orr method of treatment of wounds has been adopted by the British Military Surgeons because it has given superior results in respect to both mortality and morbidity, while casting and infrequent dressings have added to the comfort of the patients and simplified transportation and nursing care. Nonpadded casts have been used extensively, splitting the cast immediately through its entire length to allow for swelling. There have been comparatively few anaerobic infections. Air raid casualties have been 10 wounded to 7 killed and there has been much associated shock. The application

of the Roger Anderson cast-pin-skeletal fixation of fractures of femoral shafts was demonstrated.

The Effects of Roentgen Therapy Upon Gas Gangrene: Clinical and Experimental Observations, Guy A. Caldwell (by invitation), New Orleans.—In guinea pigs x-ray therapy has little or no effect in either preventing or altering the course of induced *Clostridium welchii* infections. The excellent clinical results of this therapy as reported in the literature are open to question because in the majority of the reported cases the diagnosis was not established bacteriologically. Furthermore, some recent reports have failed to confirm the earlier ones. It would seem desirable and necessary to discourage the use of x-ray therapy to the exclusion of other established methods until more conclusive evidence of its merit had been demonstrated.

Frank Meleney, New York City, stated that the Committee on Surgical Infections of the National Research Council had made a thorough investigation of reported data and was in the process of carrying out further studies. The investigation thus far has shown that x-ray therapy does have a definitely beneficial effect upon the course of *Clostridium welchii* infections.

The Treatment of Shock From the Physiologic Point of View, C. H. Best (by invitation) and **D. Y. Solandt** (by invitation), Toronto.—The etiology of shock and therefore its therapy has not been completely solved. Hemoconcentration with a reduction of circulating blood volume are the physiologic results of plasma loss into extracellular spaces and body cavities plus, in some instances, blood loss. Although the correction of hypoproteinemia and the restoration of normal blood volume by the administration of blood plasma usually restores normal physiologic relations, it is not a complete solution of the problem. Cortical extracts of the suprarenal gland seem to have influence upon the permeability of the capillaries and there is evidence that this extract aids in the treatment of shock and when given preoperatively or before shock is induced experimentally, lessens the degree of shock and delays its onset. It is possible that neurogenic factors, anoxia histamine and other histotoxins, potassium and other toxic substances play a part in the production of shock. Serum is as satisfactory as plasma for use in treatment. The method of lyophilizing plasma was demonstrated.

Norman E. Freeman, Philadelphia, presented experimental data showing large losses of plasma into the gastrointestinal tract after trauma and a reversal of the loss following administration of adrenal cortical extract. **Roy McClure,** Detroit, described the simple inexpensive method of drying plasma used at the Henry Ford Hospital. The method was reported in *Surgery, Gynecology, and Obstetrics* in 1940.

The Clinical Value of Preserved Blood Plasma, Earle B. Mahoney, by invitation of **John J. Morton,** Rochester, N. Y.—Four hundred injections of pooled lyophilized plasma have been given intravenously without regard to the type of the recipients' blood. The incidence of reactions to the blood plasma has been less than 2 per cent and none of the reactions have been severe. The rediluted plasma has been used in combating shock resulting from trauma, hemorrhage, and burns with apparent beneficial effects on the circulating blood volume. It has been of value in treating the hypoproteinemia resulting from prolonged anorexia, infection, and liver disease. It has been especially valuable in maintaining the fluid balance in the operative and postoperative patients. The advantages of the use of plasma lie in its immediate availability for emergency use, the safety and simplicity of storage, and the freedom from the necessity of typing and cross-match-

ing with the recipients' blood. Plasma is as effective as whole blood in the treatment of hemorrhage and hemophilia. It is more effective than vitamin K in the immediate control of hemorrhage in hemorrhagic disease of the newborn.

The Role of Adrenal Cortical Hormone in the Treatment of Patients With Severe Burns, Walter Estell Lee and (by invitation) **Jonathan E. Rhoads** and **William A. Wolff,** Ph.D., Philadelphia.—Consecutive determinations of the hematocrit and plasma protein concentration in patients with extensive superficial burns make it possible to estimate the probable loss of protein from the circulating plasma and to evaluate the ability of the vascular tree to retain added plasma at various times following the injury. The observations obtained indicate that the abnormal capillary permeability lasts about forty hours. During this period attempts to restore the volume of the circulating plasma to normal result in a temporary increase in the rate of plasma loss from the circulation.

The administration of adrenal cortical hormone enabled the capillary bed to retain substantial amounts of transfused plasma protein twelve to eighteen hours earlier in a majority of instances. Chloride retention in the patients thus treated was so marked that the administration of physiologic saline solution in amounts usually regarded as conservative became hazardous. The combination of adrenal cortical hormone with frequent or continuous infusions of plasma under rigid laboratory control has made it possible to carry patients with as much as 65 per cent of the body surface burned through the period of fluid shift. Evidence has been obtained that the extravasated plasma protein returns to the circulations by the fourth day after the burn. Laboratory evidence of liver and renal injury was obtainable at about this same period even in patients with relatively mild burns.

The cortical extract, estrogen, has been given in doses of 5 c.c. to 6 c.c. per kilogram of body weight every three or four hours. Plasma shift is seldom reversed without treatment in less than seventy-two hours. With adequate plasma transfusions the plasma volume can be returned to normal in one-half the time and the return can be accelerated to one-third or one-fourth with the additional administration of cortical adrenal hormone. The author's formula for calculation of plasma needs in hypoproteinemic patients was presented.

Alfred Blalock, Nashville, reported that animals in shock showed less fall in blood pressure and survived longer when exposed to ordinary room temperature than when they were subjected to higher temperatures.

The Prevention of Complications Following Radial Head Fractures With Injury to the Anterior Capsule, Clay Ray Murray and (by invitation) **Harrison L. McLaughlin,** New York City.—Fractures of the radial head are commonly divided into two groups, those showing separation of the fractured fragments and requiring operation, and those without separation of the fragments requiring only conservative measures. There is a third group of cases, frequently associated with posterior dislocations of the elbow, in which the radial head fragments are displaced anteriorly and in which there are clinical signs of severe damage to the structures of the front of the elbow joint. It is this group to which particular attention is called because of the extreme frequency of extensive ossification in the anterior elbow joint structures productive of prolonged and severe disability. This ossifying process, which involves the anterior capsule and the overlying brachialis anticus, may be markedly increased by the ordinary surgery used for radial head fractures.

In a series of 395 cases myositis ossificans developed in 4.7 per cent. In the 18 cases the operation was done days or weeks after injury and in 12 the radial heads were removed through posterior incisions.

This complication can be much reduced by excising the head through an anterior incision, cauterizing the tissue after the head has been removed, and leaving the fascia open. The operation should be done as soon as possible after injury.

Kellogg Speed, Chicago, stated that early motion was conducive of myositis ossificans and advised immobilization for three weeks following excision of the radial head. The use of a vitallium cap over the end of the radial shaft was demonstrated.

Dr. Murray in closing stated that aspiration of blood and serum from the site of fracture or operation shortened the period of disability.

Procaine Injection and Early Mobilization in the Treatment of Non-Weight-Bearing Fractures, L. Kraeer Ferguson, and (by invitation) **William H. Erb,** Philadelphia.—Leriche, in 1928, first proposed the theory that in sprains and fractures about joints, persistent pain occurs in response to afferent segmental impulses which produce an efferent sympathetic response. This vasomotor stimulation produces vascular or physicochemical changes in the injured area that, in turn, act as a stimulus of continued pain and produce edema and functional disability. By blocking the reflex arc with procaine solution, by injection either at the site of fracture or of the sympathetic ganglia, there is a rapid relief of pain and a disappearance of muscle spasms and joint disability. This permits early resumption of function. This form of therapy, although apparently contrary to all previous teachings regarding treatment of traumatic injuries, has proved by experience to be most effective in the treatment of certain types of non-weight-bearing fractures.

Five to 10 c.c. of 1 or 2 per cent novocain are infiltrated throughout the area of acute tenderness and normal function without splinting or support is carried on. The method is restricted to fractures in which reduction is not necessary and in which weight-bearing plays no part.

Clay Ray Murray, New York City, stressed the merits of the method and the dangers from stretching the limits of its applicability.

Vascular Injuries, J. M. Mason, Birmingham, Ala.—In a general review of surgery of the cardiovascular system the influence of recent contributions upon civil and military surgery was stressed. The use of novocain and alcohol block of the sympathetic innervation of the extremities, the employment of heparin, and the increasing availability of whole and dried plasma have greatly altered and extended the usefulness of surgery of the blood vessels.

The Conservative Amputation of Gangrenous Parts by Chemosurgery, E. R. Schmidt and (by invitation) **F. E. Mohs,** and **E. L. Sevringhaus,** Madison, Wis.—Chemosurgical amputation of gangrenous toes and parts of feet involves chemical fixation of the affected tissue by zinc chloride prior to amputation. After a gangrene-free level is reached, a thin layer of fixed tissue remains for a week or two. On separation it leaves well-vascularized, germ-resistant granulations. Bones and tendons are removed a week or so later. Epithelization is rapid. Scars are smooth and pliable. Of 55 gangrenous lesions involving the feet of 51 patients, healing occurred in 60 per cent after conservative chemical amputation, in 66.6 per cent of 45 cases of diabetic, and in 25 per cent of 8 cases of senile arteriosclerotic gangrene. Lack of healing was usually due to failure of the final layer of fixed tissue to separate. If the basal layer fails to begin to separate within ten days after chemosurgical amputation, the chances for healing are poor, but the patient is still in as good or better condition than before for surgical amputation at a higher level. In this series of conservative amputations chemosurgery was observed to have the following advantages: (1) preservation of a usable foot in a majority of cases and

(2) lack of operative mortality. The presence of an inflammatory reaction is indicative of a favorable prognosis, and absence of pulsations in the distal arteries is no contraindication to the use of the method. The formula of this zinc chloride paste and a description of the technique of its application appeared in the February, 1941, *Archives of Surgery.*

Minor Causalgia Following Injuries and Wounds, John Homans, Boston.—This peculiar state is characterized by hyperesthesia to pinprick and scratch and is often associated with edema and cyanosis. It arises unpredictably from minor injuries such as bruises, fractures, punctured wounds and bites, especially when infected. It may also follow thrombophlebitis. A whole limb, a finger, or a part of the hand may be affected, especially the anatomical part served by a particular nerve such as the median, ulnar, or radial. The disorder is apparently a vicious sympathetic reflex traveling centrally along the nerves serving the blood vessels and reaching the sympathetic by way of a segment of spinal cord. The diagnosis is confirmed by the temporary relief secured by local injections of procaine or sympathetic block. The treatment of this disorder consists in breaking up the vicious reflex by local injections of procaine into a "trigger point," by removing sensitive scars, and by periarterial or paravertebral sympathectomy.

Edwin P. Lehman, Charlottesville, Va., cited cases cured by local excision of scar and of foreign bodies. **James White,** Boston, recommended that before radical surgery is undertaken the response to novocain block should be ascertained. By early conservative treatment radical procedures may be avoided.

Mediastinal Parathyroid Tumors. Experience With 15 Out of 54 Cases of Hyperparathyroidism, Oliver Cope by invitation of **Edward D. Churchill,** Boston.—Fifty-three cases of hyperparathyroidism have been proved by operation at the Massachusetts General Hospital. Another was explored unsuccessfully; the tumor was found at autopsy lying in the anterior mediastinum in front of the right auricle. Of these 54 cases, adenomas were found in the anterior mediastinum in 10, in the posterior mediastinum in 5. Eight cases had been explored unsuccessfully before coming to this hospital; the adenomas were found in the neck in only 2, in the posterior mediastinum in 1, in the anterior mediastinum in 5. The uncovering of parathyroids in the mediastinum, therefore, presents a major problem. Blind search in the anterior mediastinum is often unsuccessful since a small tumor may not be felt and tumors have been found below the reach of fingers. Parathyroid exploration is now, therefore, divided into two stages: first, the neck and posterior mediastinum are explored; second, the mediastinum is exposed to direct vision by splitting the sternum.

In the presence of an adenoma the uninvolved parathyroid glandules are pale and atrophic, appearing much like fat.

Frank H. Lahey, Boston, noted that a knowledge of the normal and abnormal locations and appearances of these glands is necessary for carrying out a systematic search for a tumor. Occasionally the tumor is found within the substance of the thyroid gland.

Chronic Ulcerative Colitis: A Summary of Evidence Implicating B. Necrophorum as an Etiologic Agent, Lester R. Dragstedt and (by invitation) **G. M. Dack** and **J. B. Kirsner,** Chicago.—The bacterial flora of the colon was studied in patients with ulcerative colitis both before and after deviation of the fecal stream. Flora at first was found to be predominantly aerobic; after deviation it became almost exclusively anaerobic, and one organism, *B. necrophorum,* predominated.

This organism has been found in the diseased colon in a great majority of patients examined and isolated in pure culture in a mesenteric lymph gland and a portal thrombus. Specific antibodies have been found in the blood of ulcerative colitis patients, but not in the blood of normal individuals. A number of different strains of *B. necrophorum* have been isolated and antibodies to the specific strain found in the colon have been present in greater concentration in the patient from whom the strain was isolated than in other patients with the disease. *B. necrophorum* has been found to be more plentiful in the isolated colon during periods of exacerbation of the disease and less numerous during periods of quiescence.

It is probable that the original ulcers in the bowel are produced by other microorganisms or factors and that *B. necrophorum* is a secondary invader.

Frank Meleney, New York City, questioned the etiologic relationship of this microorganism to the disease and was inclined to consider it a secondary invader. In a search of 40 cases of ulcerative colitis *B. necrophorum* was found in only 3 cases, but in these 3 cases good responses were obtained from zinc peroxide therapy. The microorganism was found in infectious processes remote to the colon in 9 cases which did not have ulcerative colitis.

Observations on the Cause and Treatment of Postoperative Atelectasis and Bronchopneumonia, Henry K. Ransom and (by invitation) **Cameron Haight,** Ann Arbor, Mich.—The retention of secretions within the bronchial tree is responsible for the development of atelectasis and bronchopneumonia which together constitute the chief cause of respiratory complications. Careful attention to the cough mechanism in order to provide for the complete evacuation of sputum at all times greatly decreases the incidence of these complications. An impending atelectasis or pneumonia can be recognized more promptly by physical examination than by roentgen examination. The morbidity and mortality of postoperative complications of bronchial etiology are considerably lessened by the prompt use of tracheobronchial suction when the cough mechanism is insufficient to provide adequate bronchial drainage.

Tracheobronchial suction is accomplished by passing a small catheter into the nasopharynx, and then with the tongue drawn strongly forward it is advanced into the trachea quickly during inspiration. By arranging the position of the patient the catheter can be directed into either bronchus as desired. Suction is exerted through the catheter. Occasionally it is necessary to resort to bronchoscopic aspiration.

Elliott Cutler, Boston, stated that the incidence of these pulmonary complications showed a close relationship with the degree of reduction of vital capacity following operation. Such reductions of vital capacity result from painful and other stimuli emitting from the wound. Thus, total anesthesia of the wound during the first few days by some long acting agent would do much to prevent postoperative pulmonary complications. Dr. Ransom presented statistical evidence that the type of abdominal incision (transverse versus longitudinal) does not significantly alter the incidence of postoperative pulmonary complications. **Walter E. Lee,** Philadelphia, believes that the incidence of atelectasis has increased as a result of more prolonged operations and advocates the routine use of aspiration of the larynx and trachea before moving patients from the operating table. **Frank Lahey,** Boston, emphasized the necessity of training resident surgical staffs to meet the emergency of evacuating bronchial secretions in these cases immediately.

The Syndrome of Mesenteric or Subperitoneal Hemorrhage (Abdominal Apoplexy), Alson R. Kilgore and (by invitation) **Glenn F. Cushman,** San Francisco.—With diffusion of blood between the leaves of the mesentery there are at first annoying abdominal and back pain, soreness, restlessness, diffuse tenderness,

and sometimes a definite or indefinite abdominal mass. These attacks may subside at this stage and may recur or there may be progression of hemorrhage with collapse and alarming shock. Recovery is usually accomplished with complete rest and conservative treatment, but only once has the diagnosis been made preoperatively. Mindful of the syndrome it should be possible to make the diagnosis from signs and symptoms more often. At operation bleeding vessels have been identified and ligated.

Dallas B. Phemister, Chicago, stated that hemorrhage into the mesentery not infrequently occurs in association with acute pancreatitis.

The Relationship of Lesions of the Cystic Duct to the Pathogenesis of Cholecystitis, W. H. Cole and (by invitation) **E. O. Hughes** and **M. V. Novak,** Chicago.—Often chronic partial obstruction of the cystic duct can be demonstrated in the gall bladders of patients with cholecystitis.

Partial obstruction at the cystic duct was produced by one of two methods: (1) cutting a flap at the neck of the gall bladder, allowing it to protrude into the lumen at the junction of the cystic duct and the gall bladder; and (2) inversion of the wall at the neck of the gall bladder by "tuck" stitches. In over three-fourths of the cases, definite thickening of the entire gall bladder wall, simulating cholecystitis in human beings, was obtained, but only after the lapse of several months' time. Cultures of the walls of these gall bladders were positive in practically all instances. Control animals in which similar procedures were performed in the dome of the gall bladder were negative for evidence of thickened wall, etc., except at the local point of operative trauma. The experiments do not contradict other mechanisms of producing cholecystitis such as lymphatic spread, etc., in the pathogenesis of cholecystitis, but in reality are supplementary, supposedly representing the initial lesion which might bring about the infection.

Dallas B. Phemister, Chicago, raised the question of priority: May not cholecystitis as seen in man develop first and extend to the cystic duct producing the narrowing and other changes found in these ducts? Mucoceles have been found in which there were no stones and no obstruction of the cystic duct. Nathan Womack, St. Louis, referred to his experimental studies in dogs showing that aspirated gall bladder bile merely concentrated to one-half its normal volume and then reinjected into the gall bladder caused the changes characteristic of cholecystitis to develop both with and without demonstrable evidence of infection. It is possible that partial obstruction of the cystic duct produces cholecystitis because the obstruction may result in abnormal concentration of the gall bladder bile.

A Useful Method of Anastomosis of the Gall Bladder or Bile Ducts to the Gastrointestinal Tract, Vernon C. David and (by invitation) **Roy E. Brackin,** Chicago.—A technique was presented for anastomosis between the biliary and gastrointestinal tracts. Dogs autopsied as long as one year after anastomosis showed no contracture of the anastomotic opening, no dilatation of the ducts, and no evidence of liver damage. The technique has been used with success in a difficult case of biliary tract disease.

The principle of the technique consists of placement of strangulating sutures between the approximated walls of the gall bladder or bile duct and the stomach or bowel. Following necrosis of the strangulated tissue an anastomosis is established.

REVIEW OF THE SECTION ON SURGERY OF THE AMERICAN MEDICAL ASSOCIATION

CLAUDE E. WELCH, M.D., BOSTON, MASS.

THE following are abstracts of papers read before the Section on Surgery of the American Medical Association in Cleveland on June 4, 5, and 6, 1941.

Carcinoma of the Stomach in a Large General Hospital, Frederick F. Boyce, New Orleans.—Carcinoma of the stomach is a very serious problem in the Charity Hospital, New Orleans, because negroes form a high percentage of the patients. Two series of 200 surgical cases, one of which was reported in 1933, and another recent one, were compared. There has been no increase in the number of cases resected and no reduction in the operative mortality. Now of 30 patients admitted to the hospital, 10 are operated upon; 3 have exploration only; 5 have palliative operations; 2 have gastric resections. The mortality of gastrectomy is 56 per cent. This is a gloomy picture, and probably can be improved only by the careful attention of the physician, and prompt recourse to surgery, since no cooperation can be expected from the patient.

Malignant Lesions of the Stomach: Importance of Early Treatment and Results, Waltman Walters, H. K. Gray, and **James T. Priestley,** Rochester, Minn.—All of the cases of carcinoma of the stomach observed in the Mayo Clinic from 1907 to 1938 were reviewed. A third of the patients with resectable lesions had symptoms suggestive of the ulcer syndrome. Eighty-one per cent of the patients with an ulcer history had had adequate response to medical therapy. Of the resected specimens the x-ray diagnosis was carcinoma in 75 per cent, ulcer in 10 per cent, gastric lesion, unspecified, in 13 per cent, benign lesion in 1 per cent, and no lesion in 1 per cent. In 20 per cent of the cases stated by the radiologist to be inoperable or of doubtful operability, resections were possible. Of all the cases of carcinoma of the stomach admitted, 58 per cent were explored; resections were done in 26 per cent of the total. The mortality in 2,772 resections was 16 per cent. The mortality increased with age. The mortality according to type of resection was Billroth I, 11 per cent; Billroth II, 18 per cent; anterior Polya, 18 per cent; posterior Polya, 15 per cent; segmental resection, 16 per cent; local excision, 10 per cent; total gastrectomy (27 cases), 67 per cent. The survival rate (based on operative survivals) was 29 per cent at five years, 20 per cent at ten years, 15 per cent at fifteen years, 11 per cent at twenty years, and 6 per cent at twenty-five years. The five-year survival rate for lesions localized to the stomach was 45 per cent; if there was extension that was resectable, without metastasis, 39 per cent; if metastasis without extension, 17 per cent; with both metastasis and extension, 17 per cent. According to the pathologic grade, the survival rate was 86 per cent for Grade I; 59 per cent for Grade II; 30 per cent for Grade III; 23 per cent for Grade IV. The survival rate was approximately the same in all age groups.

George T. Pack, New York City, in the discussion, emphasized the fact that the skill of the surgeon is entirely secondary to an increased number of resections so far as increasing the number of five-year cures is concerned. The statistics presented by Dr. Walters, he said, formed the most optimistic report ever made

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on the control of carcinoma of the stomach. **A. W. Oughterson,** New Haven, Conn., reviewed carcinoma of the stomach as a community problem. Only 57 per cent of the patients dying in New Haven of gastric cancer from 1931 to 1938 were ever admitted to a hospital; 10.7 per cent had had resections done, and 2.1 per cent of the total represented five-year cures. More attention should be paid to patients with a short history of gastric symptoms; they should be admitted immediately for study. **Robert Zollinger,** Boston, summarized 217 cases observed in the Peter Bent Brigham Hospital in the last ten years; 85 per cent of the patients were operated upon; the rate of resection has increased to 46 per cent in the past five years. There were 8 five-year survival (38 per cent of the resected cases). **Walter O. Palmer,** Chicago, emphasized the fact that the control of cancer depends upon the patient, physician, x-ray man, and the skill of the surgeon.

The Effect of Hot and Cold Applications to the Abdominal Wall and Also Hot and Cold Fluids Administered by Mouth on Gastric and Intestinal Secretory and Peristaltic Activity, J. Dewey Bisgard, Omaha, Neb.—The effects of hot and cold drinks and applications on peristaltic activity were determined by balloons in the stomach, small intestine, and colon. Peristalsis is markedly reduced after operations on the stomach and remains so for about a week. This suggests that the stomach acts as a "pacemaker" for intestinal peristalsis. Peristalsis is increased if ice is applied to the abdominal wall and decreased if hot packs are used. By mouth, ice water decreases peristalsis and increases the hydrochloric acid output of the stomach; hot water produces the opposite effect. If ice is applied to the extremities, peristalsis is not accelerated, but the hydrochloric acid secretion still is increased. Hot packs therefore seem to be indicated for peritonitis and bleeding ulcers.

James M. Winfield, Detroit, discussed the applications of these principles and the treatment of adynamic ileus. He uses the Miller-Abbott tube, and heat externally, but does not advise pitressin. **Charles W. Mayo,** Rochester, Minn., pointed out that the most effective drugs are not necessarily the most expensive.

The Miller-Abbott Tube in Surgery, Octa C. Leigh, Jr., and **Richard O. Diefendorf,** New York City.—The importance of the Miller-Abbott tube was illustrated by its use in several types of diseases. Two hundred and seven cases of uncomplicated small bowel obstruction were treated, with a mortality of 5.3 per cent. In the cases of obstruction with peritonitis, the mortality was 16 per cent if the tube passed the pylorus; if it could not be passed, the mortality was 38 per cent. The tube has been used for the treatment of ileus, and as a prophylactic against obstruction, in appendicitis, and as an adjunct to resection of the colon, especially of the right side. The Miller-Abbott tube has not decreased the mortality of strangulating obstructions, which must be recognized and subjected to immediate surgery. Of 400 attempted small bowel intubations, there has been failure in only 10 per cent.

Grover C. Penberthy, Detroit, in the discussion, emphasized the importance of the recognition of strangulation. In addition to the advantages of the Miller-Abbott tube listed by him several years ago, its value as a prophylactic against postoperative obstruction following colon resections has now been made clear.

The Local Use of Powdered Sulfanilamide in Infections of the Peritoneal Cavity, R. Sterling Mueller and **James E. Thompson,** New York City.—Intraperitoneal sulfanilamide has been employed in 90 of the 268 cases of appendicitis treated in the Roosevelt Hospital, New York City, since January, 1940. There

were no deaths. This included 31 cases of acute appendicitis, 18 with abscess, and 41 with peritonitis. One case of jaundice was observed, but there were no other complications ascribable to the drug. In a control series of 742 cases from 1935-1939, there were 21 deaths of which 13 were due to peritonitis. This was a mortality rate of 0.53 per cent for simple acute appendicitis, 6.78 per cent for appendical abscess, and 11.96 per cent for appendical peritonitis. The sulfanilamide was sterilized by dry heat for two hours at 140°. In severe infections, the maximum dose used has been 18 Gm., of which two-thirds was placed in the abdominal cavity and one-third in the wound. The usual dose was 175 mg. per kilogram of body weight. Drainage was employed in the usual fashion. Absorption is maximum about twelve hours after operation, although the drug can be detected in the blood twenty minutes after operation, and persists about 200 hours. No bad effect on wound healing was observed. In 16 cases, administration was continued after the operation.

The Use of Sulfanilamide in the Peritoneum: Experimental and Clinical Observations, Howard C. Jackson and **Frederick A. Coller**, Ann Arbor, Mich.—The authors found that sulfanilamide, implanted intraperitoneally in dogs, provided a peak blood concentration in three hours, regardless of the amount of the dose. Mixing with gum acacia did not slow the rate of absorption. If the drug is given by mouth, the blood level is still rising at the end of twenty-four hours. Clinically, intraperitoneal implantation has been done in 67 instances (33 colon operations, 15 stomach and small bowel resections, 12 perforated appendices, and 5 of other peritoneal infections). The dose was usually 5 Gm. Twenty-nine of the patients had chemotherapy by mouth as well. Postoperatively only 5 cases showed evidence of peritonitis; it was felt that too little drug was given to 3; a pelvic abscess developed in 1. Jaundice did not appear in the patients who received only intraperitoneal implantation, but did in 31 per cent of those who received additional oral chemotherapy. No fatal results occurred from this complication. It was also proved experimentally that concentration in the portal blood is much higher than in the jugular for the first four hours after implantation. Sulfanilamide crystals could be found up to two hours after implantation, while after four hours the peritoneum appeared entirely normal.

Several additional features were mentioned in the discussion. **Henry W. Cave**, New York City, pointed out that sulfanilamide is a safe and effective agent to reduce peritoneal infections when given intraperitoneally; 4 to 6 Gm. are placed about intra-abdominal anastomoses. It will not, however, prevent all deaths. A traumatic perforation of the sigmoid with general contamination of the peritoneal cavity recovered uneventfully following immediate laparotomy and the use of sulfanilamide. **Alton Ochsner**, New Orleans, has not obtained as good results. He believes the drug should not be used unless there is a gross contamination. If it is to be used intraperitoneally, drainage should be omitted. He warned against the intraserous use of sulfathiazole, because of 2 cases of optic atrophy that followed. He suggested the possibility of small doses, with repetition a few hours later. **James E. Thompson**, New York City, cited the use of intraperitoneal sulfanilamide in 90 large bowel operations, with 8 deaths. It was also used as a therapeutic measure in 20 desperate cases of peritonitis with 6 deaths. **Dr. Coller** stated that no evidence of harm to the peritoneum from sulfanilamide has been discovered. The drug is not a panacea, and other surgical principles should not be forgotten just because it is used. It is not wise to use it in clean cases, such as radical mastectomies. Contaminated wounds are preferably treated by secondary closure of the fat and subcutaneous tissue. **Frederick L. Reichert**, San Francisco, experimentally has found no reaction from sulfanilamide in the peritoneum or

omentum, but some in the abdominal wall. Sulfathiazole produced some thickening of the root of the mesentery and marked reaction in the abdominal wall. Sodium sulfathiazole produced intense matting of the intestines and a bad wound.

The Surgical Management of Gall Bladder Disease as Correlated With New Physiologic Concepts, H. Glenn Bell and **Leon Goldman,** San Francisco.—The greatest improvement in the care of patients with gall bladder disease has been due to preoperative preparation. Proper attention must be paid to the general condition of the patient; tests of hepatic and renal function must be made. The preoperative diet should be high in carbohydrates, adequate in protein, low in fat, and should contain all vitamins, especially vitamin K. Fluid and electrolyte balance must be maintained. The proper time to operate must be chosen, preferably when jaundice has disappeared or has reached a level. Anoxia must be avoided during the procedure. Proper sedation kept at a minimum level, the use of cholangiography, and attention to the sphincter of Oddi are other important operative details. Postoperatively, bile salt therapy may be of importance. The statistics of the University of California Hospital for the past ten years were summarized. The over-all mortality in 435 cases was 2.5 per cent. Cholecystectomy in the chronic state (290 cases) carried a mortality of 1.4 per cent; cholecystectomy for acute cholecystitis, 3.8 per cent; common duct exploration, 5.8 per cent; and cholecystostomy, 0 per cent. The common duct was explored in about 20 per cent of the cases; it was done rarely below the age of 50 years, but frequently thereafter. An 11 per cent incidence of stones in the common duct was found. Only 1 patient who had had a primary duct exploration had to have a second. The results of cholecystectomy showed 93 per cent cured if stones were present, contrasted to 61 per cent of patients cured if there was chronic cholecystitis without stones.

Warren H. Cole, Chicago, in the discussion, stated that persistent pain after cholecystectomy is usually due to a wrong preoperative diagnosis. Infection of the gall bladder is usually chemical, rather than bacterial. He believes operation on the acute gall bladder is indicated if the temperature has not returned to normal in thirty-six hours after admission, or if the signs of infection increase.

The Use of Cotton as a Suture Material, With Particular Reference to Its Clinical Application, William H. Meade and **Carroll H. Long,** New Orleans.—Cotton was shown to incorporate the qualities of pliability, satisfactory tensile strength, a high coefficient of friction, stability on exposure to heat or moisture, and the failure to produce any great tissue reaction. The cotton sutures are sterilized by boiling twenty minutes or by autoclaving. They have been used in all types of wounds where interrupted sutures could be used and are particularly valuable in contaminated wounds. Sizes 50 to 80 may be used for ligatures. Heavy mercerized cotton is employed in ligating the pulmonary artery, etc. Since adoption it has been used in about 1,800 cases in the Charity Hospital. The percentage of infection in clean and contaminated wounds has been distinctly lower than that when catgut was used, and appreciably lower than silk. Thus of clean wounds, 4.8 per cent of the cotton, 5.4 per cent of the silk, and 19.3 per cent of the catgut became infected. Of the contaminated, 22.4 per cent of the cotton, 70.6 per cent of the silk, and 100 per cent of the catgut, developed infection. There is a tremendous financial saving when cotton is used. Comparative costs of each suture material if each were used exclusively in the Charity Hospital during one year would be cotton, $15; silk, $873, catgut, $6,528.

Donald Guthrie, Sayre, Pa., in the discussion, said that cotton compared with silk is much safer and easier to handle, the knots are more secure, the tensile

strength is greater, and no allergic manifestations develop. Sinuses in the presence of infection are rare. It is now used in hernias, breasts, thyroids, and about one-half of the clean abdominal wounds. It is much safer than catgut, since catgut is very often infected. **John M. Ferris,** Ann Arbor, Mich., cited experiments in which cotton, silk, and catgut sutures were introduced into the anterior chambers of rabbits' eyes. Nearly complete blindness developed after the catgut, while very low cell counts were encountered after silk and cotton. **Dr. Long** mentioned the use of cotton in gynecologic repairs. **J. E. Cannaday,** Charleston, W. Va., expressed his satisfaction with cotton. **Alton Ochsner,** New Orleans, illustrated the preferred method of sterilization. The sutures are first cut to the proper length and then placed in sterile test tubes and sterilized. If wrapped on rubber spools, some of the cotton fibers may be ruptured as they contract on sterilization. He prefers cotton in contaminated wounds, above all others.

Embryoma of the Kidney (Wilms' Tumor), William E. Ladd and **Robert R. White, Boston.**—A series of 60 cases of embryoma of the kidney observed in the Children's Hospital was discussed. It is a disease of the first 3 years of life. The tumors vary greatly, histologically. They are nearly always radiosensitive. Immediate operation, without preoperative x-ray therapy, is advisable, because of the danger of early metastasis. A preliminary pyelogram is taken to be sure of the presence of a normal contralateral kidney. The transperitoneal approach is preferred. The renal vessels are ligated before any mobilization of the tumor is done. The perirenal fat is removed with the kidney. Of the 60 cases, the operative mortality was 3.3 per cent; 18 patients are still living, 14 of them being probable cures. Recurrence always was noted before the eighth postoperative month, if it was to occur, except 1 case that recurred at twenty months. A two-year cure therefore seems to be significant. The size of the tumor does not appear to alter the prognosis, but younger patients have a better outlook than older. Postoperative x-ray for recurrence is of palliative value, but will not destroy all the tumor cells.

James T. Priestley, Rochester, Minn., in the discussion, stated that of 39 patients treated in the Mayo Clinic, there are 6 (15 per cent) five-year cures. He believes x-ray is of value before operation in order to diminish the size of the tumor, and also after operation. **Monroe Wolf,** New Orleans, presented microscopic slides of several cases observed in the Charity Hospital recently.

Diagnosis, a Responsibility of the Surgeon, Chairman's Address.—The chairman's address was read by **Lloyd Noland,** Fairfield, Ala. He emphasized the fact that diagnosis has often been relegated to the physician, the surgeon thereby merely carrying out the technical procedure. There has been undue emphasis placed upon operative details by surgeons. The surgeon's hand still remains the most important diagnostic tool; the history and other diagnostic methods cannot be neglected, but the surgeon's examination is the most valuable.

Cancer of the Lung of Long Duration, Alfred Goldman, San Francisco.—Case histories were cited indicating that cancer of the lung may have a long clinical course. Eleven cases were found in which the disease lasted more than two years. Adenomas occurred chiefly in young women, carcinomas in older males. Peripheral circumscribed tumors grow more slowly and offer the best chance for surgical cures.

The Surgical Approach to Hypertension, Geza de Takats and **Howard E. Heyer,** Chicago.—De Takats has employed supradiaphragmatic, infradiaphragmatic, and transdiaphragmatic splanchnic nerve sections, vascular implants to the kidney, and nephrectomy. Of the splanchnic nerve sections, the transdiaphragmatic section of

Smithwick gave the only real reductions of high blood pressure. The value and place of vascular implants to the kidney are still unclear. Nephrectomy in one case was successful for at least ten months. Early cases of hypertension respond most satisfactorily; the operation was of no value in malignant hypertension.

Reginald H. Smithwick, Boston, described his technique. He has found that of 66 cases with partial denervation of the splanchnic bed, only 9.1 per cent had good results. Of 38 cases with complete splanchnic denervation, 71 per cent had significant and persistent lowering of the blood pressure. Several of these greatly improved patients had malignant hypertension. **Peter Heinbecker**, St. Louis, doubted the necessity of so extensive denervation in early cases. **E. A. Kahn**, Ann Arbor, Mich., pointed out that of 700 cases operated upon by Peet's supradiaphragmatic approach, 33 per cent are living five years afterward.

Phlebitis and Pulmonary Embolism, Claude E. Welch and **Henry H. Faxon**, Boston.—The methods of therapy of phlebitis were considered. Emboli occurred in one-third of the patients who had deep phlebitis of the leg, and fatal emboli in 1 out of 25. The incidence of fatal emboli increased with age. The venogram is valuable as a means of diagnosis. Ligation and division of the saphenous vein is recommended for acute superficial phlebitis. For deep phlebitis, ligation and division of the femoral vein in patients over 40 years of age is indicated. Below that age, conservative measures should be supplemented by novocain injection of the lumbar ganglia. Ligation is indicated at any age if infarcts have occurred. In a group of 33 patients who have had ligation of the femoral vein, in whom there were thirty-six preoperative infarcts, only one probable infarct has been observed since operation.

Alton Ochsner, New Orleans, in the discussion, emphasized the importance of distinguishing thrombophlebitis and phlebothrombosis. In the former, relief of temperature and edema is rapid after novocain block. Pain is permanently relieved in 90 per cent of the patients after the first injection, while the fever subsides in 64 per cent of the cases within forty-eight hours. It is in the latter group that one must be on guard for pulmonary emboli, and it is here that vein ligation is important. **Conrad R. Lam**, Detroit, has treated phlebitis and pulmonary infarcts with heparin since April, 1939. Thirty-two patients who had had emboli recovered without further incident. One had a fatal embolus after treatment. Heparin can now be given cheaply enough to justify its use. **Dr. Faxon** pointed out that only 5.5 per cent of patients with fatal emboli have demonstrable phlebitis. It is therefore important that more attention be paid to the diagnosis of asymptomatic thrombosis that precedes fatal emboli.

The Mechanism of Delayed Wound Healing in the Presence of Hypoproteinemia, Jonathon E. Rhoads and **M. T. Fliegelman**, Philadelphia.—Studies on wound healing were presented. In the presence of hypoproteinemia, fibroplasia is markedly slowed in the experimental animal, provided the deficiency is produced by a low protein diet or plasmapheresis. However, if the hypoproteinemia is produced by repeated infusions of acacia solution, or if acacia is administered to dogs with low protein levels, the fibroplasia may be brought back nearly to normal. Thus nearly normal healing has been observed in some animals, in whom the serum protein was only 1.9 per cent.

Charles G. Johnston, Detroit, stated that in his cases most wound disruptions occurred in patients who had gastric or duodenal disease with diets low in vitamin C and protein. There is no therapeutic indication for the administration of gum acacia postoperatively. **I. S. Ravdin**, Philadelphia, emphasized the necessity of maintaining the anatomical and physiologic integrity of operative wounds.

Similarities and Distinctions Between Shock and the Effects of Hemorrhages, Virgil H. Moon, D. R. Morgan, Marshall M. Lieber, and **Donald J. McGrew,** Philadelphia.—The clinical manifestations of shock and hemorrhage are identical in many respects, but there are important differences. Shock is marked by an increased flow of lymph due to leakage of plasma through capillary walls. Edema, serous effusions, and visceral petechiae occur, while they are not found after hemorrhage. During shock the urine volume is decreased and contains albumin, red cells, and casts; during or after hemorrhage no characteristic changes occur. In shock, the red blood cell count is increased, while it is decreased after hemorrhage. It is suggested that contradictory findings have been obtained by other investigators because of the use of anesthetics during experiments. It is also to be noted that for animals in shock, a little hemorrhage is very dangerous.

Henry H. Harkins, Detroit, discussing the paper, stated that it is his belief that hemorrhage and shock are not the same, but that hemorrhage may lead to shock. Thus transfusions are not effective in the late stages of hemorrhage, just as the case is with shock. If the blood pressure is kept down for long periods from hemorrhage, the changes at autopsy are the same as those of shock. Even if shock differs from hemorrhage, from the point of view of the patient it makes little difference, since restoration of fluid is the only therapeutic measure available.

Traumatic Rupture of the Intestine Due to Nonpenetrating Wounds of the Abdomen, D. Henry Poer and **Ira A. Ferguson,** Atlanta, Ga., and **Edward Woliver,** Cincinnati, Ohio.—In a series of 1,476 cases in the literature, the total mortality was 72.1 per cent; the operative mortality in the 1,014 subjected to surgery was 59.5 per cent. Thirty-six cases were observed by the authors. Prompt operation was shown to be essential. Abdominal pain and tenderness were the most important symptoms. They were often insignificant at first, but increased rapidly. Nausea was the next most common symptom. The pulse rate rises steadily. Free gas under the diaphragm was rare. External evidence of injury was present in only 16 out of the 36 patients. A decision for operation must often be based on intelligent suspicion. The important operative procedures are closure of perforations, resection, and exteriorization.

W. L. Estes, Jr., Bethlehem, Pa., in the discussion, said that the low incidence of this lesion is shown by the fact that only 1.4 per cent of the cases in his clinic were those of abdominal trauma. The cases are divided into three groups. In the most severe no operation is indicated; in another, the diagnosis is easy, and immediate operation done. In the last the diagnosis is difficult. These patients must be observed by the same, competent surgeon, and a blood count made every thirty minutes. No opiate is to be given. The type of trauma that is most to be feared is a circumscribed blow, a kick or a fall against a projecting object.

Fresh Compound Fractures: Treatment by Sulfa-Drugs and by Internal Fixation in Selected Cases, Willis C. Campbell (deceased) and **Hugh Smith,** Memphis, Tenn.—The therapy employed in a series of 143 patients with compound fractures was débridement, irrigation, implantation of sulfanilamide, and closure of the wound, with internal fixation if indicated. Internal fixation was used in 42 cases; it is recognized that this enhanced the risk of nonunion, although it had no adverse effect on infection. The cases were divided according to severity of the injury. In the mild cases superficial débridement was done and the wound cleaned, but not enlarged. Pistol shots were treated as closed fractures; no probing was done for the bullet. Shotgun injuries, on the other hand, were usually associated with severe fractures. For moderate and severe cases complete deep débridement was

followed by implantation of 5 to 20 Gm. of sulfanilamide. The wounds were closed unless they were over twelve hours old, or if there was too much soft tissue damage to allow closure. Postoperatively, sulfathiazole was given at the rate of 1 Gm. every four hours as soon as nausea ceased. It was found that the percentage of nonunion was not influenced by sulfanilamide. The incidence of pyogenic infection has been reduced from 33 to 18 per cent. In the cases that became infected, the infections were not so severe as they were before sulfanilamide. The use of sulfanilamide has greatly increased the number of primary open reductions and closures.

Harold R. Bohlman, Baltimore, in discussion, emphasized the treatment of shock and the use of local or regional block, and careful wound toilet. He believes bullet wounds should be opened and carefully cleaned. Entirely too much tissue has been removed by débridement. Tension must be avoided at all times, especiaaly since gas gangrene develops as a result of disturbance of circulation. **J. E. Cannaday,** Charleston, W. Va., has found markedly improved results with compound fractures from the use of sulfanilamide.

The Splinting of Compound Fractures, Frank J. Cox, New Orleans.—The various methods of splinting that may be employed for compound fractures were described in detail. For the lower extremity, the Thomas splint with the clove hitch for traction is used. The hitch should be replaced by a skewer through the bottom of the shoe if traction is to be continued for some time. Fixed traction in open splints may be maintained by means of two pins attached to the Thomas splint. Russels' traction is to be continued for some time. Fixed traction in open splints may be maintained by means of two pins attached to the Thomas splint. Russels' traction is not advisable for compound fractures since dressings are difficult. For the upper extremity a Jones arm splint may be used for transportation traction. Traction through the olecranon is often valuable. Roger Anderson's multiple pin method was discussed.

H. A. Swart, Charleston, W. Va., illustrated a new splint he has developed for the upper extremity.

Chemotherapy in the Treatment of Compound Fractures, Rex L. Diveley, Kansas City.—Dr. Diveley presented his plan of therapy for osteomyelitis—oral administration of sulfathiazole to produce a blood level of 5 mg. for several days, followed by a thorough local operation, with local implantation of sulfathiazole, wound closure, and postoperative oral administration of the drug, usually for two weeks. Fifty-six cases have now been treated that way, of which 16 were compound fractures. Of the series, 53 healed by primary intention, 2 others healed, but extremely slowly, and 1 case was a failure. The average total dose of sulfathiazole was 57.4 Gm.; the blood concentration, 4.3 mg. per cent; the amount of drug implanted locally, 1.9 Gm..; and the healing time, 21.6 days.

Francis M. McKeever, Los Angeles, in discussion, stated that 71 per cent of 73 patients with large wounds and compound fractures developed infection. When chemotherapy was employed in a similar group, 6 cases remained clean while only one became infected. **Robert W. Johnson, Jr.,** Baltimore, advised the use of sulfanilamide in compound fractures treated early, since the gas bacillus and streptococcus are the most dangerous contaminants; in late cases, where they are known to be absent, sulfathiazole is better.

Book Reviews

Surgery of the Hand. By R. M. Handfield-Jones, M.C., M.S., F.R.C.S. Pp. 135, with 95 illustrations, including several in color. Baltimore, 1940, Williams and Wilkins Co. $4.50.

This readable little book has been clearly and concisely written. It is primarily for the general practitioner and, therefore, somewhat didactic in nature. The anatomical descriptions and drawings are clear and concise, and elucidate some points which most authors have left a little cloudy. In a few respects, the author's advice is counter to the practice in this country, such as in swabbing lacerations with iodine, omitting elevation of the extremity in lymphangitis, and elimination of toxins of infection by purgation, but on the whole, the therapy is excellent.

This book makes a pleasant evening's reading, and is indexed for reference purposes. It should be of value, both to the student and to the practitioner.

Age Morphology of Primary Tubercles. By Henry C. Sweany, M.D. Cloth. Pp. 258, with 73 illustrations. Springfield, Ill., 1941, Charles C Thomas, Publisher. $5.00.

This is a monograph of 252 pages, extensively illustrated with charts, reproductions of roentgenograms, and many excellent photomicrographs; it is the product of a great deal of painstaking pathologic work correlated with careful analyses of case histories.

Sweany's thesis is that primary tubercles, over a period of years, go through a morphologic evolution, whose stages follow, within certain limits, a definite time schedule. By studying primary lesions at post mortem in the lungs of individuals whose original contact with tubercle bacilli can be dated with fair accuracy, he constructs, in the first three chapters, a timetable for the pathologic changes which take place in these tubercles.

The next four chapters apply this timetable by estimating from it the age of calcified primary foci found at necropsy, and thus attempting, for example, to date the initial infection of an individual whose history indicates two or three separate episodes, one of which may have represented the occurrence of a primary lesion. Finally, a series of living patients is presented, in whom, through serial roentgenograms, it is possible to follow the evolution of primary infections of various types; and the author attempts to correlate these x-ray changes with the pathologic data presented earlier, but recognizes that this can be done only to a very limited extent.

In summary, then, this monograph describes a remarkably complete pathologic study of "first infection" tuberculosis, and an interesting new approach to the subject through analysis of age morphology. It seems possible that the method may become useful as a tool in studying the pathogenesis of tuberculosis in certain well-documented cases. At present (as the author himself states), this work has very little practical clinical application, but it teaches at least one valuable clinical lesson: the old calcified tuberculous focus which one assumes to be "healed," undergoes changes for many years, and in the process, it may under some circumstances become potentially dangerous as a source of endogenous reinfection.

Williams' Obstetrics: A Textbook for the Use of Students and Practitioners. By Henricus J. Stander. Ed. 8. Pp. 1,401, with 704 illustrations. New York, 1941, D. Appleton Century Co.

This eighth edition, Stander's second revision, of Dr. Williams' textbook on obstetrics continues the classic presentation of its subject matter. While much of the material has been completely revised, it retains unmistakable earmarks of Dr. Williams' style and ease of presentation. In spite of the publication of several other texts on obstetrics during the past ten years, this one persists in being head and shoulders above any other. It is ideal for the student and practitioner as well. For those not interested in historical data and theoretical considerations, these are now easily separated since they appear in small type.

Many of the original illustrations have been replaced and a host of new ones appear, all from the hand of a competent medical illustrator. The text itself has been almost completely rewritten, with the result that little of the original remains unaltered. The section on embryology now conforms to the newer ideas of Streeter and Hartman. The mechanism of labor embraces the roentgenologic findings of Caldwell and Maloy. The toxemias of pregnancy are classified and discussed according to the new classification of the American Committee on Maternal Health, a step in the direction of ultimate national standardization of the criteria for diagnosing these diseases. Roentgenologic pelvimetry is discussed in detail. The treatment of puerperal infection and certain other infectious processes complicating pregnancy and the puerperium includes the newer concepts of chemotherapy. The chapters on diseases of the urinary system and endocrinology have been virtually rewritten. Thus, this revised edition has been brought up to date with all recent advances pertaining to physiology and pathology of gestation and to medical and surgical complications of pregnancy and the puerperium.

The Role of the Liver in Surgery. By Frederick F. Boyce, M.D. Pp. 365, with 44 illustrations. Springfield, Ill., 1941, Charles C Thomas, Publisher. $5.00.

Boyce's monograph, *The Role of the Liver in Surgery*, in 1940 was awarded the quinquennial Samuel D. Gross Prize for research in surgery by the Philadelphia Academy of Surgery. The monograph was published in accordance with the stipulations of the Samuel D. Gross Prize Award. As stated in the preface, one of the stipulations of this award is that the monograph shall be the report of the research work of a single individual. As also stated in the preface, it was the express desire of the Gross Prize Committee of the Philadelphia Academy of Surgery that the monograph be presented exactly as submitted, on Jan. 1, 1940, except for minor editorial changes and the addition of new work on the bleeding tendency in newborn children (Chapter VIII).

This monograph places timely emphasis on a number of important aspects of liver function and liver disease, particularly as they relate to surgery. For example, there is an excellent discussion of the hepatorenal syndrome, which is a relatively frequent postoperative hepatic complication and which has not been given sufficient attention in the past. The relation of sulfanilamide to the production of liver damage and jaundice, both before and after operation, is quite properly stressed. This section of the monograph contains a well-rounded discussion and survey of the literature on so-called "postoperative liver death."

Considerable attention is given to the subject of assaying liver function. Boyce's past studies, as summarized in the present monograph, have dealt chiefly with the hippuric acid test. The relative merits of various methods of carrying out this test, together with the description of the actual technique, are thoroughly considered. There is no doubt that the hippuric acid test is distinctly worth while, yet its relative value may have been somewhat overemphasized in this monograph. Boyce has evidently employed but two other methods of testing

liver function; namely, the bromsulphalein and the bilirubin tolerance tests. Neither of these, of course, are of much, if any, value in the patient who is more than a little jaundiced. All three of the tests are sufficiently involved that they are not well suited to serial study. In this respect, more emphasis might well have been placed upon the value of serial qualitative urine urobilinogen tests. Boyce recognizes that it is impossible to rely upon any one test alone in the clinical study of liver function.

The monograph contains an excellent discussion of the hemorrhagic tendency in jaundiced patients, and its treatment by vitamin K. Included in this discussion is a summary of Boyce's studies of the serum volume index. These have aided greatly in clarifying the relationship between hypoprothrombinemia and the defective clot formation in jaundice.

The importance of fatty liver in increasing postoperative mortality is touched upon briefly by mention of Ravdin's important studies of this question. Some discussion of the relation of riboflavin, cholin, and lipocaic to the problem of fatty liver might well have been included.

The material composing the monograph is well organized, and the illustrations are clear, and, for the most part, well selected.

Clinical Urology. By O. S. Lowsley and T. J. Kirwin. Two volumes, pp. 1684, with 365 illustrations. Baltimore, 1940, Williams & Wilkins Co. $10 per set.

These books cover their field quite adequately. While the introduction recommends them particularly to medical students, general practitioners, and general surgeons, they will repay study by the urologist as well. The two outstanding features are the wealth of excellent illustrations by Didusch, and the rather extensive bibliographies. These two alone are worth the cost of the volumes.

There are excellent sections on diagnostic roentgenology, the simpler laboratory procedures, anesthesia, and irradiation therapy, in addition to the customary discussion of history taking, general and special instrumental examinations, and the various diseases and disorders. Surgical therapy is covered about as thoroughly as possible considering the size of the books. The discussion of prostatic surgery is remarkably temperate and sound, if one ignores the authors' recommendation of subtotal (semiradical) perineal prostatectomy in certain cases of benign hypertrophy.

The relation of diet and urinary pH to lithiasis and infection are covered.

Lest the reader suspect that the reviewer is in the pay of the authors or publishers, it is well to point out certain defects in the work. One might, I think, be justified in drawing attention to a noticeable tendency to overemphasize the works, instruments, and pet contraptions of the authors, although one must admit that others are there, too. The old fable of the danger of sudden emptying of the bladder is again handed down to posterity, together with the standard apparatus for its prevention (or for salving the physician's conscience if anything goes wrong!). Neurogenic vesical dysfunction is inadequately discussed. One could also wish that publication had been late enough to permit a discussion of sulfapyridine and sulfathiazole in gonorrhea.